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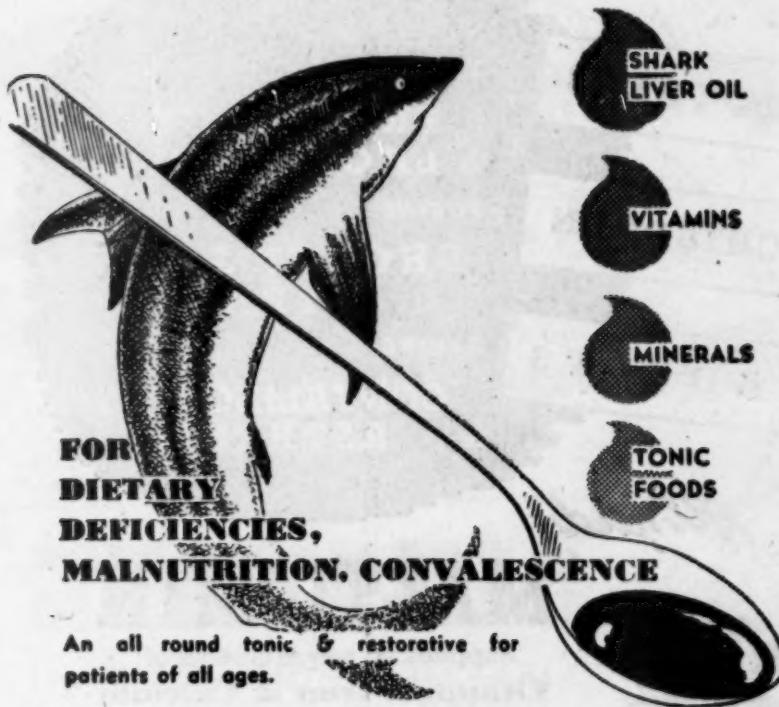
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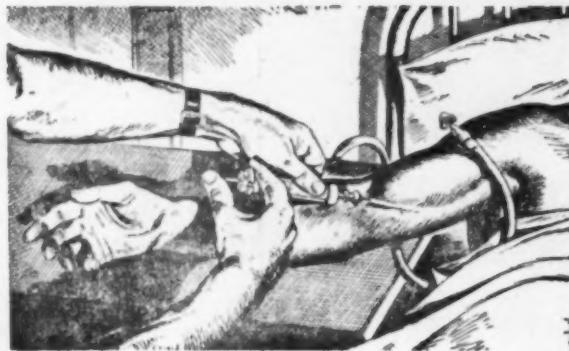
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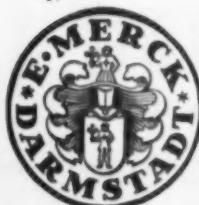
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1. Sayer, R.J.; Michel, J.C.; Moll, F.C., and Kirby, W.M.M.:
Am. J. M. Sc. 221:256 (March) 1951.

2. Bickel, G., and Platner, H.: Schweiz. med. (Jan. 6) 1951. Wehrsehr. 81:1

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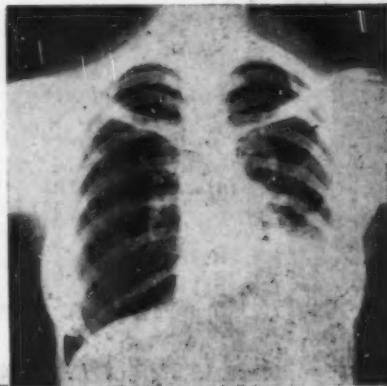
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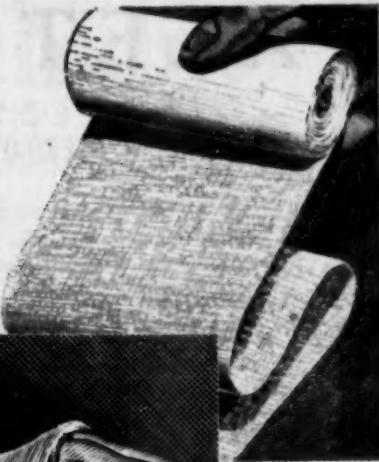
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Original Articles

GENERAL ADAPTATION SYNDROME*

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STRESS plays an important role in the modern every day life of man and the process of adaptation to the stress is constantly at work as a series of reactions on his part. The general adaptation syndrome GAS is an attempt at generalization on the basis of such known reactions. GAS forms an important trend in modern medicine and so a review of its salient features is here attempted.

The syndrome GAS attempts at integrating the results of animal experimentation and of clinical observation into a single hypothesis. Hans Selye, the exponent of this hypothesis, is a Canadian professor of experimental medicine and surgery. He attempted to produce artificially in animals pathological conditions observed in human beings. He claims to have produced rheumatoid arthritis in the ankle joints of rats by injecting formalin into the joints. The condition was greatly aggravated when deoxycortone (an adreno-cortical steroid) was injected simultaneously, and the condition was prevented from occurring when cortisone (another adreno-cortical steroid) was injected along with formalin. Similarly he was able to produce experimentally a variety of pathological conditions which were aggravated by one group of steroids and ameliorated by another group. These experiments led him to formulate in 1936, his theory of 'Alarm Reaction' which he developed into the 'General Adaptation Syndrome' ten years later.

* Specially contributed to THE ANTISEPTIC.

The principle on which the hypothesis of GAS is based, is that all living matter responds to stress by certain reactions, and the basic pattern of these reactions remains the same irrespective of the stressing agent (stressor). This uniform reaction-phenomenon constitutes the general adaptation syndrome. Aberrations in this physiological reaction to stress in the form of GAS may give rise to pathological conditions which may be grouped under the generic term 'Diseases of adaptation'. A number of heterogeneous conditions like rheumatoid arthritis, nephrosclerosis, Cushing's syndrome, arteriosclerosis, acute gastrointestinal ulcerations, Addison's disease etc. have been included under this heading. At first sight it appears incredible that these polymorphic conditions should owe their origin to one and the same cause *viz.* the GAS. But in view of the multifarious types of stress and the conditioning factors that modify the response, one cannot very lightly dismiss the probability.

In a living organism every stress evokes a defensive response having two components : one is the specific response, the other is the non-specific response. Instances of the specific defence-response are : hypertrophy of a muscle as a result of prolonged increased work, increase in the basal metabolic rate during cold weather, increase in the secretion of adrenalin in hypoglycaemia, etc. Here the stressors are, overwork, cold and hypoglycaemia, and the specific defence responses are, hypertrophy of the muscle, stimulation of thyroid, and secretion of adrenalin respectively. Specific antibody-formation may be called a specific defence response, while the alterations in the blood counts may be considered part of the non-specific defence-response. The non-specific and the specific responses may be compared to the general and particular properties of a chemical substance, say, an acid. Thus hydrochloric acid will have certain general properties in common with other acids forming a group and specific properties by which it distinguishes itself from other acids in that group.

The total response of the organism to a stress consists of a standard uniform general response, the GAS and a variable specific response. The latter varies with : (a) different stressors ; (b) differing extraneous conditions—the environment, climate, diet, previous diseases etc. ; (c) heredity ; and (d) the target organ and its state. This may be compared to the electric current producing different results like heat, light, sound, energy etc., at the periphery depending upon the target apparatus employed.

Stress is capable of producing damage as well as adaptation. Disease consists of the results of disordered reaction to stress and to the damage arising from it. Medicine has so far considered damage and damaging pathogens, and to a great extent neglected the disorders due to deranged adaptation. The doctrine of GAS will therefore, undoubtedly draw our attention to this neglected aspect of medicine.

Parts of the body which are suddenly overwhelmed by a stress of great magnitude, or those parts that are not well protected against stress by the systemic mechanism of GAS may show evidence of damage in the form of necrobiosis of cells. Waterhouse-Friedrichsen syndrome in which bilateral haemorrhages occur in the adrenals, is an example of the sudden exhaustion of GAS, under the influence of a powerful stressor.

It will be interesting to find out whether similar but minute stresses added in the reaction phase of the organism will invoke better resistance. If it is found to be true it will give support to the homoeopathic principle of treatment 'Like cures like.'

The non-specific defence response which is general and adaptive in nature, constitutes the general adaptation syndrome of Selye. This is a general 'call to arms' of the whole adaptive mechanism of the body in response to external or internal stress which may be potentially non-lethal or even innocuous.

GAS consists of three phases :—

1. *Alarm reaction (AR)*, which is produced by a continuous stress and consisting of two stages : the stage of shock, followed later by the stage of 'recovery from shock' or the stage of counter-shock. The stage of shock represents the initial submission of the organism to the stress. The stage is passive and is accompanied by hypothermia, hypotension, haemo-concentration, increased capillary permeability, hypochloræmia, transient hyperglycæmia, leucocytosis etc. The stage of counter-shock represents the mobilization of body defences, and is manifested by a fall in the eosinophil count, thymo-lymphoid involution, hyperchloræmia, and particularly by an increased production of corticoid substances.

2. *Phase of resistance* :—During this stage, the defences of the body come into full play and the enemy is held at bay.

3. *Stage of exhaustion* :—When the defence is inadequate or cannot be maintained for long, the enemy tends to gain mastery and defeat appears inevitable. Many of the changes noticed in the alarm reaction, which had disappeared during the stage of resistance, reappear as preludes to death.

General adaptation of the organism for defence against the stressor is geared by the concerted action of the hypothalamus-hypophysis system. Humoral or nervous impulses from the site under stress, warn this defence-headquarters of the imminent danger and the adaptive mechanism is set in action to prepare the organism for overcoming the stress. The adaptive defence is launched by the hypothalamus representing the autonomic system and the hypophysis representing the endocrine system.

The hypothalamus defence mechanism :—The hypothalamus working through the splanchnics of the autonomic system stimulates the adrenals into secreting more adrenergic hormones,

adrenalin and nor-adrenalin in the blood. Adrenergic stimuli are also sent to the effector or target organs. The important effect of adrenergic stimulation during general adaptation, is vaso-constriction with a rise in blood-pressure. Cholinergic discharges may take place simultaneously. The concurrent cholinergic and adrenergic stimulation of the effector organ probably helps to stabilize its function by preventing any gross deviation during stress. The autonomic system works also in other ways *viz.*, by influencing blood-sugar-water metabolism, blood counts etc.

The hypophyseal defence mechanism :—The primary response of the pituitary to the stress, is by 'a shift in the anterior-lobe-hormone production.' As a result there is a diminution in the production of the somatotrophin, gonadotrophin and the thyrotrophin hormones of the pituitary, and an increase in the production of ACTH (adrenocorticotrophin hormone). ACTH stimulates the adrenal cortex into secreting abnormal quantities of adrenal corticoids.

The adrenal cortical hormones—the corticoids consist mainly of two groups—the gluco-corticoids and the mineralo-corticoids.

The gluco-corticoids (cortisone and compound F) cause transformation of non-sugars into sugars *i.e.*, gluco-neogenesis. They also produce important changes in the blood, like lymphopænia, eosinopænia, granulocytosis, increased phagocytosis and antibody-formation. They prevent the formation of granulation tissue and the production of arteriosclerotic changes. In their activities they generally counteract the influence of the mineralo-corticoids.

The mineralo-corticoids (desoxycorticosterone and compound S) mainly influence the electrolyte balance in the blood. In other respects, they act chiefly in opposition to the gluco-corticoids.

These two main groups of cortical hormones are stimulated by two separate pituitary hormonal mechanisms. Pure ACTH is predominantly glucotrophic. The pituitary factor is predominantly mineral-trophic. It is suggested that the stress causes the adrenals to liberate cortical hormones. If there is a disproportionate overproduction of one group of corticoids over the other, diseases of adaptation appear. Generally the gluco-corticoids are the 'good fairy' and the mineralo-corticoids, the 'evil fairy' for the living organism. So the diseases created by the 'evil fairy' should be amenable, according to Selye's hypothesis, to the gluco-corticoid hormones.

Selye's hypothesis failed to rouse sufficient interest in the scientific world till September 1950 when Hench and his colleagues working at the Mayo Clinic independently reported miraculous cures of rheumatoid arthritis by cortisone. This is a gluco-corticoid isolated from the suprarenal cortex by Kendall in 1941. Soon after this report, a number of conditions claimed by Selye as diseases of adaptation, were reported to be favourably influenced by cortisone. This clinical evidence gave strong support to Selye's hypothesis and

his dream envisaged on the strength of animal experimentation came true and was realized in actual practice. The clinical experiments at the Mayo Clinic with cortisone thus helped to bring Selye's neglected hypothesis into prominence. The support which Selye's experimental conclusions obtained from Hench's clinical trials with cortisone, will remain as an outstanding landmark in the history of medicine. The stress and GAS, bid fair to stand the test of time and to revolutionize medical thought and medical concepts in the years to come.

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'Jayashree'
Deshmukhwadi, Poona City.

Treatment of Pneumococcal Meningitis with Penicillin as Compared with Penicillin plus Aureomycin

Among 43 patients with pneumococcal meningitis treated with massive parenteral doses of penicillin thirteen (30%) died. Among fourteen similar patients treated with aureomycin in addition to the same dose of penicillin, eleven or 70%, died. The last 14 of the 43 penicillin-treated patients were treated alternately with the 14 penicillin-aureomycin-treated patients. Among this control group of penicillin-treated patients there were three deaths. There was no essential difference between the two groups with respect to age, the number of organisms in the spinal fluid, mental status, portal of entry, pneumococcal complications, the presence of other diseases, or the day on which therapy was started. It is concluded that the poor results with the penicillin-aureomycin combination were not due to the chance inclusion of more severely ill patients in this group, nor did toxicity to aureomycin seem to account for the results. Rather, the evidence seems to favour the conclusion that penicillin and aureomycin are mutually antagonistic when employed together in the treatment of pneumococcal meningitis. It appears unwise to use combinations of penicillin with aureomycin, terramycin, or chloramphenicol in the treatment of patients with pneumococcal meningitis, or in the treatment of any patients, even those with milder infections in which antagonism has been shown *in vitro*. Consistently good results have been obtained in the treatment of pneumococcal meningitis with doses of 1,000,000 units of penicillin at two hourly intervals without the use of the intrathecal route. Further investigation of regimens employing insoluble penicillin salts in order to produce similar serum and spinal fluid concentrations is indicated, since these may simplify the dosage schedule.

Since good results have been obtained by the use of aureomycin therapy alone in pneumococcal meningitis, further studies should be made on the efficacy of aureomycin, terramycin, and chloramphenicol, without adjuvant penicillin in the treatment of this disease.—(Lepper, M. H., and Dowling H. F., *A.M.A. Arch. Int. Med.*, 88, 4, 489-495, 1951).

CHOLINE IN NUTRITION AND THERAPY*

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CHOLINE is a member of the vitamin B complex essential for the functioning of animal organisms. Because of its increasing importance particularly in controlling fatty livers and other associated hepatic disorders it was considered desirable to review our present knowledge regarding the functions of choline under various physiological and pathological conditions. Choline is widely distributed in nature as a component part in the phospholipid molecule. An approximate idea of the choline content of various food materials is given below.

Choline content in various food materials in mg. per gramme.

Material	Choline	Material	Choline
Wheat	0.92	Egg yolk	17.13
Polished rice	0.88	Milk powder	1.09
Peas (dried)	1.88	Fish	0.87—2.0
Potato	1.06	Lamb shoulder	1.19
Spinach (sun-dried)	2.38	Beef liver	0.30
Cabbage	2.5	Lamb kidney	3.6
Soyabean	3.0	Ham	0.88

The importance of choline in nutrition has been recognized only in recent years after Best¹ had demonstrated its role in the prevention of fatty liver in depancreatized dogs. Besides being considered essential for the growth and lactation² of experimental animals when placed on diets free of choline, or its precursors, the animal showed characteristic symptoms which included fatty degeneration of the liver, renal lesions, ocular haemorrhages, regression of the thymus etc. It has been observed that a condition of fatty and enlarged liver is often a precursor of cirrhosis and other diseases of the liver in man. The study of the function of choline and other lipotropic factors has been augmented by findings concerning the influence of other dietary factors on the metabolic functioning of the liver. These concepts have revolutionised the basis of early methods of therapy, particularly those which advocated the use of extremely restricted diets. Today, nutrition-therapy in hepatic diseases is considered an essential adjunct to all routine medical and surgical treatments. The essence of the modern therapeutic diet in liver diseases is the provision of liberal amounts of calories proteins and carbohydrates, reduced amounts of fat, supplements of B vitamins and the lipotropic factors such as choline, its precursors and related compounds.

* Specially contributed to THE ANTISEPTIC

Relationship between choline and methionine.—The discovery of the relationship of choline to methionine resulted from the fact that both these substances were able to prevent the accumulation of fat in the liver or cause the disappearance of such liver-fat if it had already accumulated. After Best and his associate³ demonstrated that the fatty liver induced by feeding a low-protein high-fat diet could be prevented by the addition of choline to the diet, Tucker and Eckstein⁴ found that methionine was equally effective as a lipotropic agent. This behaviour of methionine was later demonstrated by Vigneaud and others⁵ to be related to its ability to function as a transmethylating agent whereby it yields the methyl groups which enable the aminoethyl alcohol readily synthesisable from glycine to be converted to choline. Thus in rats, mice, dogs and probably in man also, methionine can partly subserve the important function of a dietary substitute for choline. The reverse process of the formation of methionine from choline under some dietary conditions has also been proved by studies with isotopically tagged molecules. Though choline cannot replace methionine in the diet and although homocystine (a demethylated form of methionine) did not sustain the growth of rats on a choline-free diet, choline *plus* homocystine was found to be effective in place of methionine⁶. It has been actually shown by du Vigneaud and others⁷ that under such conditions choline worked as a transmethylating agent, methyl groups of choline being transferred to homocystine with the resultant synthesis of methionine. Thus, the requirement of choline and methionine will vary according to the levels of protein and choline-containing substances present in the diet.

Considerable research work has been done in recent years to find out the adequate level of choline and methionine in the diet required for growth and maintenance. The growth-stimulating effect of dietary choline in young rats in contrast to the absence of such an effect in older animals has been explained by a preferential utilization of methionine for growth in the older animals⁸ so that the addition of choline does not decrease the demand on the available supply, whereas in the young animals several metabolic processes are active in the overall utilization of the amino-acid; and the introduction of choline in the diet supplies the needed methyl groups for at least some of the processes, thereby releasing methionine for growth. Thus, the greatest stimulation for growth by choline was obtained at 200 mg. level. Unless adequate amounts of choline are supplied, a low protein diet may bring an acute deficiency of choline superimposed on a deficiency of essential amino-acids. On high-protein diets (methionine-rich) however, the choline requirements of rats may usually be largely satisfied by the methionine present in the diet. It may be presumed that no sharply preferential affinity for methionine is possessed by the biochemical reactions concerned with protein synthesis as compared with reactions occurring in the transformation of methionine to choline⁹.

Function and metabolism of choline.—The role of choline in nutrition may be divided into two categories:—(a) the utilization of the intact molecule of choline; and (b) its ability to furnish a labile methyl group. The growth-promoting effects of choline in young rats, its ability to form lecithin and its effect in preventing fatty livers and haemorrhagic kidneys are believed to be due to the whole molecule of choline. As a transmethylating agent it furnishes labile methyl groups which are transferred to homocystine to form methionine and thence to glycoxyamine to form creatine. This capacity of choline is similar to that of methionine and betaine though under certain conditions these two substances cannot wholly replace choline. The function of choline in preventing hepatic cirrhosis must be distinguished from that of cystine and methionine in preventing hepatic haemorrhage and necrosis¹⁰. The observation that betaine under certain conditions was only a third as effective as choline in the prevention of haemorrhagic kidney-syndromes in rats has been explained by assuming that only one of the three methyl groups of betaine was labile¹¹. The mechanism of lipotropic activity of choline is believed to be tied up with the functioning of the intact choline molecule and that of methionine is explained on the basis of its available methyl groups which permit the synthesis in the body, of choline from non-methylated precursors. It is considered likely that choline exerts its lipotropic effect by stimulating the rate of turn-over of phospholipid formation on the liver specifically, by being incorporated into newly-formed lecithin molecules. This explanation is based on the current belief that phospholipid formation is an essential pre-requisite to fat transport and utilization. That it actually does stimulate the rate of phospholipid turn-over has been demonstrated by means of tracer technique¹² & ¹³. It is important to realise that while labile methyl groups are essential for the synthesis of choline, they are not essential to the phenomenon of lipotropisms, the lipotropic effect being dependent more upon the entire structural unit of the compound.

Little, however, is known of the fate of choline after oral or intravenous administration. A recent report¹⁴ indicates that though choline is not excreted significantly in the urine of a normal person, almost two thirds of the orally administered choline is excreted as trimethylamine, due to bacterial transformation of choline in the intestine. In liver diseases, however, the urinary trimethylamine elimination after choline administration is delayed or decreased. The authors suggest that the bacterial flora of the intestine is possibly altered in the patients with hepato-biliary diseases in a quantitative and/or qualitative manner, which might explain the reduced formation of trimethylamine in these conditions. Studies on the urinary excretion of intravenously administered choline may give results which can be correlated with the results of utilization of orally administered choline as measured by the phospholipid turn-over with P 32¹⁵.

Interrelationship of choline, vitamin B_{12} and folic acid.—A large volume of work has been done in recent years regarding the possible role of vitamin B_{12} and folic acid in the utilization of choline or choline precursors for the maintenance of normal liver fat, prevention of renal damage and promotion of growth in experimental animals^{16,17}. In the presence of sub-optimum levels of choline or methionine, both B_{12} and folic acid afford complete protection against kidney damage thus showing choline-sparing action¹⁸ and since they seem inter-related, the requirements of one of these nutrients cannot be established unless the levels of the other two are taken into consideration. The authors suggest that in the treatment of megaloblastic anaemias it may be advantageous to consider the use of all the three nutrients. The same group of workers have recently reported that the reduction of the choline requirement for the maintenance of liver by B_{12} and folic acid may be due either to the biological synthesis of additional choline or to the increased utilisation of the choline¹⁹. Schaefer and Knowles suggest that folic acid functions primarily in methyl synthesis and B_{12} functions in either the transfer or the utilization of labile methyl²⁰.

Role of other nutrients.—The experimental production and control by means of diet, of fatty liver and ultimately of liver necrosis and cirrhosis represents one of the major advances of modern times in the diagnosis and treatment of diseases of the liver. Besides the activity of lipotropic factors the role of other nutrients like protein, fat and vitamins in the metabolism of the liver cannot be ignored and liberal amounts of calories in the shape of carbohydrate and protein must be added. Inadequate absorption, metabolism and storage of the vitamins is a common result of liver diseases. Deficient dark adaptation (vitamin A deficiency), osteoporosis (D deficiency), prolongation of blood-clotting-time (K deficiency), have all been recorded as common complications of chronic liver-diseases. The provision of extra-supplies of these vitamins by oral or parenteral administration therefore, becomes necessary. The requirements of the B-vitamins are likewise heightened in liver diseases, as the damaged liver not only interferes with absorption of the vitamins but may also fail to store or even metabolise them. Mere supplements of these vitamins may not always correct the effects of their deficiency; excess amounts must be provided.

Clinical uses of choline.—Encouraged by the results of animal experiments, which demonstrated the effect of choline and other lipotropic substances on the production of cirrhosis of the liver on the one hand and the arrest of the conditioned preservation of the liver on the other, clinicians applied the principles to human sufferers from cirrhosis. In a survey of 247 cases of cirrhotic patients extending over 10 years, Steigman²¹ found that a diet high in protein and carbohydrate but low in fat supplemented by choline or methionine proved to be very effective as judged by the lower mortality rates.

Other beneficial effects besides fat-removal, were noticed as a result of this therapy. A significant number of patients did not however, respond to lipotropic-therapy and the author considers that those cases perhaps represented cirrhosis of a type not due to nutritional deficiency. Several cases of hepatic cirrhosis characterised by ascites and large palpable livers^{22, 23} treated with choline-chloride in doses varying from 1.5 to 6 gm. daily, (with added cystine and inositol in some cases) showed clinical improvement; e.g., elimination of the ascites and increase in the serum-protein-level. As small doses (even up to 5 g. daily) of choline or methionine were found ineffective^{24, 25}, in the treatment of functional disorders of the liver, which accompany infectious hepatitis, a daily dose of 20 g. choline-chloride for 2 to 3 weeks has been suggested; the use of such a high dose however, usually leads to ketosis. Choline was found effective (given intravenously 1 g. daily in a 5% solution) in patients with pernicious anaemia who had failed to respond to purified liver extracts²⁶. It was concluded, that an adequate amount of the anti-pernicious anaemia factor was stored in the liver but not effectively elaborated because of the fatty state. As has been summarised by Jukes (*loc. cit.*) "the complex nature of cirrhosis and its grave prognosis, make it difficult to accumulate clear-cut data with respect to the amelioration-effect of any dietary ingredient but results to date indicate that supplementation with choline is a desirable adjunct to supportive treatment".

Requirement :—As stated earlier, the choline requirement of a normal adult depends on the content of methionine and other related substances in his daily diet. On the basis of a 100 mg. *per* 100 g. of ration, which is usually adopted in animal experiments, the choline requirement of an average adult man would be about 500 mg. daily. In diseased and pathological conditions however, much higher than this maintenance dose would be necessary. Doses of 20 mg/kg. body-weight was found necessary to prevent the appearance of fatty liver in animals²⁷ and the curative dose must necessarily be 3 to 4 times more. On this basis the curative dose for a man of 70 kg. (140 lb.) would be about 6 g. daily but may have to be 3 or 4 times more in some cases. "The effective curative dose must approach the toxic dose, the danger being a sudden flooding of the circulation with choline and a consequent depression of the heart and blood-pressure," was the conclusion reached by the *British Medical Journal*²⁸.

Choline has also been administered intravenously both in animals and in man during recent years. Cats can tolerate 15 mg/kg. body-weight without toxic effects while 30 mg. produces a reversible arrest of respiration and 35 mg resulted in death²⁹. As the material was rapidly destroyed in the body, 0.8—0.9 mg/kg. body-weight (in 0.2 to 0.4% solution per minute) may be injected practically indefinitely. (This dose would correspond approximately to 3 g. *per* hour

in man). For intravenous therapy a daily dose of 1·0 g. in a 5% solution was found to produce the minimum unpleasant reactions, and so it may be continued for as long as 2 weeks. Higher doses (5 or 10 gm. as 1% slow drip-infusion over 3 hours) were usually accompanied by nausea, vomiting, sweating, abdominal discomfort and depression³⁰.

Summary.—Choline is a member of the vitamin B-complex, essential for the proper functioning of animal organisms. Besides being essential for growth and lactation its value in the prevention of fatty liver and haemorrhagic renal lesions has been demonstrated in experimental animals. Where the deficiency persists the fatty liver is followed by cirrhosis and other hepatic diseases. The action of choline is thus mainly directed against the deposition of excess fat in the liver. Under some dietary conditions choline can replace methionine and *vice versa*, because of their ability to serve as transmethylating agents. The requirement of choline therefore, depends on the level of protein (methionine) and other related substances present in the diet.

Some inter-relationship has also been observed between choline folic acid and vitamin B₁₂. In the presence of sub-optimum levels of choline or methionine, both B₁₂ and folic acid afford complete protection against kidney-damage thus showing choline-sparing action.

The exact requirement of choline is not known. Since choline is widely distributed in nature as a phospho-lipid complex, the average human diet usually contains 250 to 600 mg. Based on animal experiments the curative dose for an average adult man may vary from 6 g. daily to 3 or 4 times as much, depending on the severity of the pathological condition; but these higher doses may approach the toxic level. Besides oral administration, choline has been administered intravenously also to animals and men during recent years; a daily dose of 1·0 g. in 5% solution has been found to produce the minimum of unpleasant reactions. But higher doses (5 to 10 gm.) have been found to cause nausea, vomiting, sweating, depression etc.

Clinical evidence is accumulating to show that some types of liver-cirrhosis, particularly those of nutritional origin, are often favourably influenced by choline. The effect seems to be more pronounced when choline is combined with folic acid and vitamin B₁₂. The diet however, should be rich in proteins. Supplementation with choline therefore, is a desirable adjunct to supportive treatment.

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Tuberculous Abscesses and Empyema following Penicillin Therapy

Arce and Villota report 13 cases of tuberculous abscesses following intramuscular injections of penicillin and 4 cases of tuberculous empyema following intrapleural administration of penicillin in therapy of pneumococci purulent pleurisy. The tuberculin test gave negative results before the development of the tuberculous disease and became positive after it in nearly all the cases. The clinical course of the disease was typical of the primary infection in all the patients. Many were infants who had not been exposed to infection and some had been under constant medical care. "The aetiological role of penicillin in the production of tuberculous abscesses and tuberculous empyema cannot be doubted in the cases we report" say the authors. They emphasize the necessity for bacteriological examination and guinea pig inoculation of the pus of all apparently sterile abscesses that appear in the course of penicillin treatment and of the pus from patients with purulent pleurisy that seem to be aggravated by penicillin therapy.—(*Rev. Espan. Ped.*; *Abst. J.A.M.A.*, 21:7-1951).



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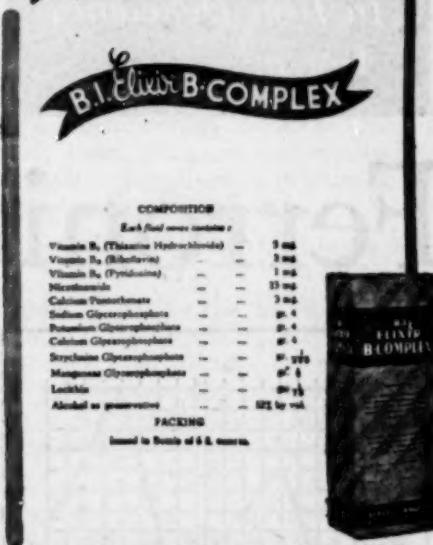
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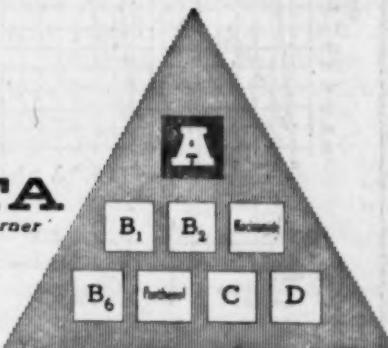
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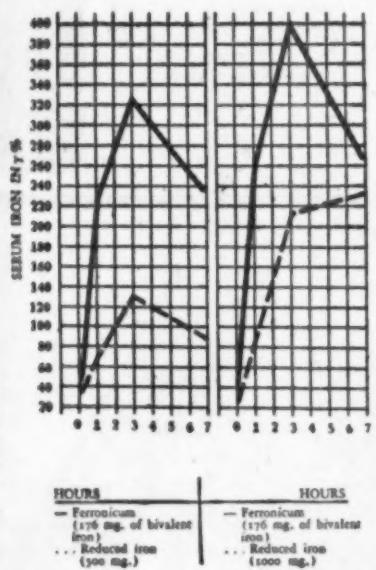
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ASCARIASIS*

V. RAMAMOHAN RAO, L.M.P. (Madras),
Honamakonda, via Kasipet Station, N.S. Ry.

DURING the past twenty five years I have treated a large number of cases of *Ascariasis* under varying conditions and presenting symptoms which simulated several other diseases, e.g., pneumonia, typhoid, pulmonary tuberculosis, rheumatism, cerebral malaria, acute abdomen, multiple neuritis, meningitis, dengue, excitement, epilepsy, rectal irritation, peptic ulcer, colic, diseases producing sub-normal temperature, puerperal sepsis and pleurisy.

I have invariably diagnosed ascariasis by the following signs and symptoms:—

(1) Crepitatory sounds on auscultation at the navel or in the area immediately above it (abdominal auscultation); (2) twitchings especially during sleep; (3) excitement; (4) bluish conjunctiva with sweats, if in a child; (5) pain in the region of the navel; (6) protuberant abdomen which neither sags entirely nor shows up unduly prominent while the patient is reclining; and (7) transitory loss of consciousness.

I attach particular importance to the crepitatory sounds heard on auscultation of the abdomen at the navel or just above it, as this was invariably present in 99% of my cases. I dewormed a patient on the tenth day of continuous fever with haemorrhage, which had been diagnosed as typhoid by the attending physician. The result was dramatic. The patient passed a round worm and soon became normal. I treated a boy aged four years who was sweating profusely and whose conjunctiva was found to be bluish. The boy was given santonin. He passed two worms on one day and one more worm later, and was soon all right.

Some children have protuberant abdomens while others have not. Protuberant abdomen in children is due to:—(1) Pot-belly, in which the belly sags down when the child assumes the reclining posture; (2) infantile liver, in which the upper abdomen is prominent in sharp contrast to the lower, except when complicated by ascites; (3) worms, in which the abdomen neither sags down entirely as in (1) above, nor shows a sharp contrast as in (2) above.

In the case of children without protuberant abdomens, diagnosis of ascariasis is somewhat difficult, as several other conditions have to be ruled out. Ascariasis often simulates several other diseases. Some of these will be dealt with below, in the shape of case reports.

I. *Ascariasis simulating pneumonia* :—A boy aged 9, had high temperature and cough. The pulse-respiration ratio was upset.

* Specially contributed to THE ANTISEPTIC.

There were definite signs of pneumonia in the right lung. The sputum was neither rusty nor stringy but frothy; it showed no pneumococci. Crepitatory sounds could be heard over the navel. Urine was free from albumen. Santonin was given and the boy passed a number of round worms and was immediately all right.

II. *Ascariasis simulating typhoid* :—A girl aged 12 years had continuous fever for ten days; there was a sudden intestinal haemorrhage and this was certainly unusual in enteric after 10 days. The crepitatory sounds (navel) were heard and the W.B.C. count showed 10,200; it was therefore, diagnosed as a case of ascariasis; santonin expelled the worms and the haemorrhage stopped. The temperature also came down to normal. Another peculiar case was that of a boy S., aged 14, who had continuous fever. The temperature headache, and restlessness were all typical of typhoid. But I noted certain other peculiarities:—(1) The boy threw out his tongue before becoming unconscious, and after a transient spell he would talk complainingly. (2) There were frequent flushes in the face. (3) The boy was always in an excited mood. I therefore, sought for and found the crepitatory sounds in the region of the navel. I was then sure of my diagnosis. In order to be quite sure, a WBC count was made. That stood at 9400. Santonin and Mag sulph did not bring out the worm. The case then simulated pneumonia and there was also irritation. The neck muscles were stiff. There was hyper-excitability of the reflexes. But there was no Kernig's sign. Another dose of santonin was given. He began to improve though he did not pass any worms. The flushes and also the excitement continued although meningeal trouble abated. He became constipated. I gave him Mag sulph in solution. He passed broad motions in one of which he passed a round worm. The flushes then disappeared and also the excitement. The worm left the intestines only after a month, inspite of repeated doses of santonin followed by a purge.

III. *Ascariasis simulating pulmonary tuberculosis* :—A well built adult with remittent fever and cough accompanied by puerile breathing here and there, was diagnosed as a case of pulmonary tuberculosis. The patient was advised to go to Madanapalli. On the way, when he had reached Bezwada his temperature suddenly shot up; feeling very nervous he returned home. On the night of his return he felt a severe burning sensation in his abdomen and abnormal hunger. He stealthily entered the kitchen and ate rice with mango pickle to his heart's content. Next morning he passed a round worm and became free from all symptoms!

IV. *Ascariasis simulating rheumatism*.—A young boy, aged 7 years, had a swelling on the right wrist. There was neither fever nor any other sign of inflammation excepting the pain. I had previously treated all his sisters for worms. Crepitatory sounds over the navel were present. He passed a number of worms after

santonin, and got over his trouble. I saw similar cases subsequently and found that they all had an affection of the right wrist.

V. *Ascariasis simulating cerebral malaria* :—G., aged twenty-five had fever of 102.8°F with repeated convulsions. There were also signs of bronchitis. He was becoming conscious between the attacks of convulsions. Convulsions in malaria at his age and for that comparatively low temperature are not usual or common. Suspecting worms, I treated him for ascariasis and he passed a large number of worms and was cured.

VI. (a) *Ascariasis simulating acute abdomen* :—At a monthly meeting of the doctors of Nair's Hospital in Bombay, which I once attended, a surgeon of that hospital described a very interesting case. The patient progressed very satisfactorily for nine days after a short-circuit operation on the intestines. On the night of the ninth day there was a call for him from the hospital saying that the patient was sinking. He thought that the stitches might have given way, and opened the abdomen and put his hand in. He felt something twisting on his finger which to his great surprise was a round worm.

(b) *Ascariasis simulating appendicular abscess* :—G. B., aged 18 years had fever, nausea, vomiting, pain and tenderness at MacBurneys point, and swelling of the size of a small apple; and her right thigh could not be extended. Asked whether she was constipated, she said that she was having small and frequent motions of a liquid consistency. I auscultated the abdomen and heard numerous crepitations. After taking her blood for WBC count I gave her penicillin empirically and as a measure of caution. The WBC count was 12000. The swelling had assumed the size of a big apple. On the next day she passed a number of seat worms in her diarrhoeic stools. The swelling was still the same, although her pain was less. Then I gave her Sodii sulph. In one of the motions, she passed a round worm. From the next day onwards the swelling began to subside and in three days' time she was able to walk. With anti-anæmic treatment she became quite all right.

VII. *Multiple neuritis simulated by ascariasis* :—R., aged 32, complained of numbness and pricking and darting pains in her legs. I elicited tenderness in the calf-muscles. On further investigation she told me that her hands twitched now and then and that she experienced jerks in her body. I made abdominal auscultation and heard the crepitatory sounds. Santonin and purge brought out the worm. The pains which resembled multiple neuritis subsided after the treatment.

VIII. *Ascariasis simulating meningitis* :—I was called to see a patient aged 50 having 103°F, with a low muttering delirium, stiff neck and hyperexcitability of the reflexes. There was no Kernig's sign. There were abdominal crepitations, and a drooping jaw. The

back muscles were not stiff. This kind of incongruity is noticed in a case of worms. This case was treated by an unqualified person and the patient died.

IX. *Ascariasis simulating dengue* :—Mrs. V., had an attack of fever which, to all intents and purposes, looked to be remarkably like dengue. I told the patient and her husband that it was dengue. On the fifth day of the fever the patient suddenly vomited and brought out a round worm along with the vomit. The temperature fell and the patient was all right.

X. *Ascariasis simulating excitement* :—K. K., a boy of 15 had a peculiar shake-up. I had an urgent call at night and I found that the patient was greatly excited and there was a big crowd of people around him singing *Raghupathi Raghava Rajaram* to soothen his nerves. I put the boy to bed and cajoled him into sleep. The later reports stated that punctually at 9 p.m. the boy would jump out of bed, become restless and finally get scared. I elicited further that the boy used to go to bed at 8-30 p.m. and would get excited punctually at 9 p.m. I wanted to break this (9 p.m.) periodicity; so I was with the boy from 8 p.m. and did not allow him to go to sleep till after 9-15 p.m. There was no excitement till then. I thought I had mastered the situation. But at 9-45 p.m., he got the attack. Now it was plain that the first half hour of sleep was responsible for the attack. This twitching in sleep is a recognisable sign in persons harbouring round worms. I then auscultated the abdomen and found the crepitations there. I prescribed santonin and a purgative. The boy passed a lot of pin-worms, but not the round worm. After giving him santonin thrice subsequently the boy passed a round worm. The excitement became gradually less and finally disappeared in a week's time.

XI. *Epilepsy simulated by ascariasis* :—M., aged 14 years was having epileptic attacks numbering five on some days. In between the attacks the girl twitched a lot. There was paresis of the left leg and left hand. The left side of the body alone used to perspire. The right side of the body was warmer than the left. These twitchings in between the attacks, suggested to me the presence of round worms. With no more help or clue, I made bold to give santonin. The result was that the girl passed a number of round worms and got rid of her attacks of what were mistaken for epileptic fits.

XII. *Ascariasis causing rectal tickling* :—A gentleman came to me and told me that he had taken santonin 7 times. "Every time the worm appeared to come down into the rectum and returned back" he said. I made a P. R. and felt the tail at one time. I conjectured that the worm was having its hold higher up and that it was sending its body and tail downwards. Under chloroform, I dilated the rectum and as soon as the tail appeared I caught hold

of it with an artery forceps and then applied two more, one above the other. The worm was brought out to the great relief of the patient.

XIII. *Ascariasis simulating peptic ulcer* :—A woman aged 18, had a slight evening rise, pain over the epigastrium and slight icterus. She then developed nausea and vomiting. The irritation of the stomach was so terrible that even water was not retained. Nothing relieved her. There was no tenderness in the epigastrium. The pain was slightly relieved by gentle massage over the epigastrium. She appeared acutely ill, and would not leave her bed all the twenty four hours. The abdominal crepitatory sounds were there. How to expel the worm when the stomach was so irritable was the question. Luckily for her a worm was passed without any intervention ; gradually nausea and vomiting disappeared, but the patient had become anaemic.

XIV. *Ascariasis simulating colic* :—A boy of 12, suffering from colic for over 4 months was diagnosed by the crepitations over the navel to have ascariasis. Santonin worked well and the boy was relieved of his colic.

XV. *Ascariasis simulating diseases producing subnormal temperature* :—A child of five, was brought to me for 'coldness' of the body, and sweats. Pulse and respiration were normal. Temperature was 95°F. The temperature had been like that for fifteen days, during which period hakims had tried to raise the temperature by stimulants, but in vain. I heard crepitatory sounds over the navel. I decided not without some hesitation, to give santonin along with some stimulants. Santonin was accordingly given and the result was not alarming. Stimulants were continued even after the expulsion of the worm ; but the temperature did not come up to normal till after a week had elapsed.

XVI. *Ascariasis simulating puerperal sepsis* :—Mrs. V. N. had temperature, restlessness, sweats and a foul-smelling discharge. The signs and symptoms resembled those of a case of puerperal sepsis. Her bowels were constipated for five days, so she was given an enema. In the returning fluid two round worms floated out. After this the smell in lochia disappeared ; the temperature touched normal ; and the woman had a sense of well-being.

XVII. *Ascariasis simulating pleurisy* :—A goldsmith in Madikonda had pleuritic pain in his left chest. The rub was distinct. He had to be sitting in one particular position for four days and four nights. He could neither bend, nor lean, nor even move without bending the back. Morphia did not relieve the pain. In fact the patient grew worse. He had nausea all the time. On the fifth day he got up all of a sudden and demanded fowl, mutton, and pots of milk etc. He then developed twitchings. I took the clue

and gave him santonin and a purge. He passed the worm and was soon well again.

Conclusions.—Diagnostic clues:—Crepitatory sounds are invariably heard over the navel in ascariasis. Twitchings especially during sleep are confirmatory. Bluish conjunctiva in a boy with sweating over the whole body is suggestive; bluish conjunctiva in a child perspiring only over the head suggests rickets. Bluish conjunctiva in an adolescent who is lean and lanky, would suggest tuberculosis. Transient loss of consciousness in remittent or intermittent fevers suggest ascarasis.

The Control of Gastric Acidity

"Gastric hydrochloric acid is the greatest known hindrance to the healing of peptic ulcer" (Sippy). The inadequacy of most forms of therapy in controlling acidity is well known. Aluminium hydroxide gel and magnesium trisilicate when given hourly failed to neutralise the gastric hydrochloric acid for more than a quarter of an hour—this conclusion has been reached by many independent observers. All alkalis given by mouth, even in large doses, have such a transient action as to be valueless. Hitherto the most effective method of neutralizing stomach contents over long periods has been the continuous intra-gastric milk and alkali drip introduced by Winkelstein (*Amer. J. Surg.*, 15, 523). This is usually well-tolerated by patients but has practical disadvantages. Drs. Douthwaite and Shaw of the Guy's Hospital, London hit upon the method of providing sucking tablets containing milk solids and alkali. Accordingly a tablet was prepared which could be conveniently lodged between the cheek and the gum, would dissolve slowly and yet satisfactorily depress the gastric acidity. It was palatable to the patients, was 1 inch in diameter and 1/5 inch in thickness and consisted of:—Solids from whole milk combined with maltose and dextrins 40 grains; magnesium trisilicate 3.5 grains, mag. oxide 2 grains, calc. carbonate 2 grains, mag. carb. 0.5 grain, and ol. menth. pip q.s. If lodged between the gum and cheek it was found to take 20 to 30 minutes to dissolve and its food value was about 11 calories. The authors tested these tablets on eleven patients, with suitable controls, and found that the continuous sucking of these tablets *between meals*, starting half an hour after each meal and continuing till going to sleep was the most convenient and effective method of neutralizing gastric acidity. Their effect was more prolonged than that obtained by any of the customary forms of alkali therapy, apart from milk-alkali drip. It is suggested that the continuous sucking of these tablets (which were prepared for the authors by Messrs. Horlicks Limited) will hasten cure and prevent relapse of peptic ulcers.—(*Br. Med. Jour.*, 26-7-1952, pp. 180-182).

THE PUBLIC HEALTH SERVICES IN THE UNITED STATES OF AMERICA*

A. K. ANWIKAR, M.P.H. (Johns Hopkins University),
*Curator, Dept. of Social and Preventive Medicine, Medical College,
Nagpur, Madhya Pradesh.*

THE Public Health Service of the United States is 153 years old today and is the principal agency of the Federal Government for the nation's health, operated under laws passed by United States Government.

The Public Health Act of 1944 established the basic organisation of the Service, consisting of four statutory bureaus, viz. : (1) the Office of the Surgeon-General; (2) the National Institutes of Health; (3) the Bureau of Medical Services; and (4) the Bureau of State Services. The administration is vested in the Surgeon-General, and an Assistant Surgeon-General, who is appointed from the members of the commissioned corps. These four administrative units are responsible for specific functions. The Surgeon-General's office is the bureau of business management. The National Institute of Health controls Scientific Research, the Bureau of Medical Services administers the programmes for hospital medical care and related activities, and the Bureau of State Services attends to the cooperative federal state health programmes. The work of Research, Clinical and Public Health Practices, is executed through (a) the National Institute of Health; (b) the Bureau of Medical and State Services; the organisational structure of these services reflects two main concepts. One is the flexibility which enables the services to adapt to rapid advances in scientific research and development, and the second is the consideration that related programmes are best administered by grouping them together from the stand point of major emphasis on clinical research and improved public health practice.

The function of the office of the Surgeon-General is personnel administration, budget and fiscal administration, supply, business—management of public health services and the operation of the divisions of international health and public health methods. The records for the year 1950 show that the U.S.P.H.S. administered approximately 321.5 million dollars (about 1607.5 million rupees) in appropriations and authorizations. Eighty per cent of this amount was allocated to agencies and institutions in the form of grants. Fifteen per cent was spent on the entire operations of the U.S.P.H.S., including hospital and medical care programmes, quarantine services, in-service research activities, and technical aids to the States. The remaining five per cent was the budget for providing the needed facilities for the public health services. During that year the full-time employees of the services numbered 16,300, and a part-time

* Specially contributed to THE ANTHROPOCIC.

staff consisting of consultants, and Members of the National Advisory Councils listed 747 persons. The commissioned corps of the P.H.S. comprised 1,185 officers of the regular corps and 967 reserves. These included physicians, dentists, scientists, nurses, dietetitians, pharmacists and physiotherapists.

The National Institute of Health which carries out the major part of the research programme, is located on 300 acres of land near Bethesda, Maryland. This great institute includes sections on (1) cancer, (2) microbiology, (3) heart diseases, (4) dental research, (5) mental health, (6) arthritis and metabolic diseases, and (7) neurological diseases and blindness. The laboratories are up-to-date and extensive and are the finest in the world today. It was in the year 1930 that the parent institute first came into existence, and seven years later, a cancer section was added. The National Mental Institute was established in the year 1946, and then followed a rapid expansion by the formation of the Heart Institute (1948), Dental Research Institute (1948), Institute for Neurology and Blindness (1950). The Division of Arthritis and Metabolic diseases was also established as full-scale Institute in the year 1950. A clinical centre with 500 beds was under construction during my visit in the year 1950, and was scheduled to reach completion by 1952. This is designed to permit basic experimental research and clinical studies of the different problems under investigations. The staff and facilities for medical care, physiotherapy, recreation, spiritual ministry, and social welfare, compare very favourably with those provided in the best hospitals anywhere else. In the fiscal year 1951, the combined budgets of the National Institutions of Health amounted to 46 million dollars (230 million rupees). The Americans consider that their very survival as a free nation depends on the progress of their scientific knowledge and therefore, lay great stress on their research programme. Both in their own laboratories, and in their support of investigations in hundreds of other centres they are helping to increase the Nations Research-man power, as well as its ability to combat diseases.

The Bureau of Medical Services

This Bureau operates the Hospitals and the out-patient Medical care system for legal beneficiaries of the Public Health Service. It also assists the States and Communities in the construction of Hospital and Health facilities and also aids in the development of Medical Hospital Nursing, and dental resources. The average daily census of patients was 7,470. In order to afford improved care to the patients, training programmes are conducted at the hospitals, residencies for physicians, and dentists, and through on-the job informal teaching to maintenance-personnel. Further, about 150 clinical research studies are encouraged at the P. H. S. Hospitals every year. One of these projects is the study on tumour, conducted

at the Tumour Clinic at the Marine Hospital, Baltimore, Md. with the cooperation of the Cancer Institute.

The Bureau of Medical Services is concerned with administration of the National Hospital Construction programme and survey. Financial assistance, technical advice, and professional leadership are made available to State and the local Governments, as well as to non-profit organisations so that community needs for hospitals and other health-facilities may be measured and met. This Bureau is also concerned with foreign quarantine programme, i.e. examination of conveyances, goods, and persons arriving at the sea and border points of entry.

The Bureau of State Services

The chief function of this Bureau is (1) Prevention of diseases; and (2) Promotion of good health for all the citizens. It serves and works with health agencies of the states to improve individual and community health by assisting states and local communities to strengthen and expand their health programmes. Besides the financial grants-in-aid the Bureau offers advice, consultations, and technical assistance to state and local agencies on many health matters. Some divisions of this Bureau investigate new public health techniques and conduct demonstrations which point the way for state and local action. The services of specialists are lent to the state and the local health departments to help solve specific problems and to conduct training courses, seminars and other educational programmes for state and local health personnel. The Bureau also collects and publishes health statistics, to enable the states to note the trends and determine future courses of action. The Bureau is made of sixteen divisions and centres and are essentially organised in three major groupings: (1) Personal health services for control of communicable and chronic diseases, and to improve community health. (2) Environmental health services for control of external factors in our environment which affect our health. (3) Staff and administrative services to handle internal management and functions which help states apply and use such necessary services as public health education, public health nursing, vital statistics and the grant-in-aid system. The high lights common to the various divisions of the public health service are; (a) sodium fluoride demonstration programme; (b) multiphasic screening; (c) the division of chronic diseases; (d) the division of venereal diseases; (e) tuberculosis; (f) some of the tests which are commonly included in the multiphasic screening are X-ray for tuberculosis, and other chest pathology, hearing and vision tests, urinalysis for diabetes, blood pressure for hypertension, measurements for height and weight, and blood tests for syphilis and anaemia.

The function of the communicable disease centre is mainly epidemiological survey to trace the course, incidence, and transmission of

specific diseases. Malaria has been most successfully eradicated in the U.S.A. and quite a successful campaign has been launched for control of murine typhus fever, tuberculosis and venereal diseases.

Public Health Methods and International Health

This division started as an office for statistical investigations is concerned today with the application of sound statistical methods to a wide variety of public health problems, chiefly in the field of social sciences. The U.S.P.H.S. has assisted in many ways the pan-American sanitary organisation, and the institute of inter-American affairs. During the past year the health programmes were in operation in Greece, Liberia, Indo-China, Iran, Paraguay, Peru, Korea; health-missions are also sent to the under-developed areas of the world under the "Point four programme".

Public Medical Programme

The roll of the Government whether federal, state or local in providing medical care, is presented under four general heads:—

1. Medical care supplied to groups for whom the government has assumed complete responsibility.
2. Programme for prevention or treatment of specific types of illness or disability such as cancer, tuberculosis, mental or chronic diseases, permanent injury or deformity.
3. Programmes of general medical care services, primarily for the needy.
4. Programmes affecting the health of the entire population.

*Groups served by the federal programmes:—*The federal government assumes complete responsibility for the supply of medical services to certain very large groups, principally to members of the armed forces, to veterans, to members of the merchant marine, to its Indian wards, to the inmates of the federal prisons, to persons who become disabled in government service, and to certain groups which vary in size and character with changing economical and political conditions. The service rendered by the federal government to these various groups may be given by physicians at government expense. It may be given in hospitals owned or operated by the federal government or in general or special hospitals which contract to accept such patients.

*Armed forces:—*Complete medical care is provided to members of all the armed forces and for certain of their dependents. The services include health examinations diagnostic procedures, consultation, treatment and hospitalization. If the facilities for army and navy are found to be inadequate, they are supplemented through civilian resources. The total strength of the armed forces in U.S.A. in the year 1949 was 1,492,000, i.e., approximately 1 per cent of their population (148-millions). In the year 1945 this

number shot up to nine times, *i.e.*, the total army was 12,364,000. It is estimated that during peace time at any given period, about 22 per cent of the active-duty strength will be hospital-patients. The hospital care is provided through 48,642 beds in 119 army, navy, and air-force hospitals.

Veterans :—The number of living veterans of all wars in the United States as on June 30, 1950, was in excess of nineteen millions or 12·7 per cent of the total population. Complete medical and dental care is provided to any veteran with a disability incurred in line of duty or aggravated by military service. This care includes both hospital and out-patient service and provides complete treatment, medical appliances, pharmaceuticals and all needed special services, such as physical therapy, and rehabilitation services. Hospital is also provided for non-service-connected illness if a bed is available and if the veteran is financially unable to pay the cost. The veterans administration operates its own general and special hospitals and also purchases a substantial volume of care from civilian hospitals and private physicians and dentists in private practice. The total cost of medical and hospital care for veterans exceeded 500 million dollars in the fiscal year 1949-50. A programme for the construction of new hospitals, estimated to cost three-quarters of a billion dollars is under way. This will provide 67 modern hospitals with a total of 38,600 beds. During September 1949 five of the new hospitals reached completion; 39 were under construction and 23 were in the planning stage.

Members of the Merchant Marine

Since 1798, the government of the U. S. has provided general medical care for the sick and the disabled naval men. Operated by the public health service for this purpose, there are today 24 marine hospitals. Eighteen out-patients dispensaries, and ninety-six medical relief stations. These provide hospitalization, general, medical and dental care, and also the preventive health services, for more than 200,000 American merchant sea-men, the members of the U. S. Coast Guard, and certain other beneficiaries of the service.

Indians :—The Bureau of Indian affairs in the United States Department of the Interior, provides health services for some 400,000 Indians on the reservations in the U.S.A. and Alaska. Those services include health examinations, dental care, and both in-and out-patient care in hospitals and in the the sanatoria. There are 61 hospitals for Indians with a total bed capacity of 3,343. The cost of health facilities and activities of the Indian services exceeded 5 million dollars in 1945.

Prisoners :—In co-operation with the Bureau of prisoners, the Public Health Service furnishes medical, dental, and psychiatric services, in the 27 federal penal and correctional institutions, and during the year 1947, care was provided to 34,000 federal prisoners.

An additional 107,000 prisoners in state penal institutions also receive medical care through the government.

Other groups :—The National Leprosarium at Carville is operated by the public health service, and is open to any citizen infected with leprosy. Hospitals are maintained at Lexington, Kentucky, Fortworth and Texas, for care of persons addicted to narcotics and for certain types of mental diseases. To meet certain temporary needs, the federal government has organised a very considerable number of emergency medical services, of one sort or another. One of these was the emergency maternity care to the wives of men serving in the four lowest grades of the military forces. Medical care is also afforded to their children under one year, under-law-provision by the Congress in 1943. During the year 1945 this programme provided comprehensive service to almost 1.5 million mothers and infants at a total cost of 127 million dollars. At its height it is estimated that one out of every seven births in the nation was served under this programme.

Programmes for Specific Types of Illness

It was during the First World War that the government considered it desirable to assist the states in setting up a programme for the prevention of venereal diseases in the civilian population, as part of a broad effort to prevent the development of these diseases in the armed forces. This received enormous support from all the states and although funds were withdrawn after the war, much of the progress made was maintained by the states at their own cost. The Congress allotted a substantial sum for control of V.D., in the year 1938. This served as an impetus to different states. Working on this experience the federal government made an appropriation in the following years, for similar campaigns in the field of tuberculosis, cancer, heart and industrial diseases, and psychiatric disorders.

Mothers and children :—The passage of the Shepard-Tower Act in the year 1921 marked the beginning of the activity of the federal government towards improving the health services of the country as a whole. Increasing sums were made available by the Congress in the succeeding years, which suggests that these services were welcomed by the people as effective and essential. Public law 734 was passed in the year 1950 and this enabled the Congress to increase the grants to states from 11 million to 16 million. Grants for the crippled children's programme were also increased from \$ 7.5 millions to \$ 15 millions; the different states rendered further contributions, which enabled the public health departments to extend still more elaborate and extensive services to mothers and children. The programme for crippled children includes services in the fields of medical, surgical, diagnostic and treatment services. In the year 1948, 175,000 crippled children received benefit of this

programme, and of these 30,000 patients spent about two million days in hospitals or convalescent homes.

Tuberculosis :—In the United States a total of 83,470 beds are provided for tuberculosis, and these are operated by different agencies as follows :—

The Local Governments operate 44 per cent.

The State operates 31 per cent.

The Federal Government operates 12 per cent.

The non-governmental agencies operate 13 per cent.

A broad programme for X-ray screening has been developed and as many as 14 million persons received the benefit of this programme, during the year 1949-50.

Mental diseases :—In the year 1949 the states provided 705,423 hospital beds for the mentally ill patients. This constitutes about 49 per cent of all the hospital beds. The operation responsibility is shared by different agencies in the following proportion :—

The States own and operate 84 per cent.

The Federal Government operates 9 per cent.

The Local Governments operate 4 per cent.

The non-governmental agencies operate 3 per cent of them.

No fees are collected from the patients, for the service rendered, except in some few states. Mental clinics are established as a part of the general hospitals in most cities, with a view to detecting early cases, and giving them the benefit of close observation, guidance and such treatment as may be necessary. The National Mental Health Act passed in the year 1950, authorised grants to the states, to the tune of \$ 3,550,000 for development of mental hygiene clinics and child guidance-services in local communities. In all but sixteen states, the Health Department has been officially designated as the mental health authority to develop mental hygiene clinic services, under the provisions of the Mental Health Act.

Chronic diseases :—The problem of chronic diseases has attained its present dimension due to the following factors, viz.: (1) aging of the population over a longer span of life due to improved living-conditions; (2) the discovery of improved methods for prevention and treatment of most of the acute illnesses, and (3) education and consequent activities which eliminate accidents and hazards leading to premature death. In the past, cities and countries maintained alms-houses to take care of the aged and the infirm-poor. Some states have provided more systematic and elaborate facilities in the form of chronic hospitals and nursing homes to meet the needs of the chronically ill persons. Out of the many problems of the present day, cancer is the most important one. The government plays a significant role by launching a methodical campaign for

early detection and treatment of these cases. An elaborate service is offered to the population through the National Cancer Institute, and federal grants to non-profit institutions for cancer-research, and to health departments for cancer detection and consultation clinics.

Vocational rehabilitation

The vocational rehabilitation office of the Federal Security Agency, provides technical and financial services through the state-agencies to persons who may be handicapped physically or mentally. In such cases where financial eligibility is established according to specifications provided under law, any and every type of medical care is extended inclusive of medical, psychiatric, surgical examination or treatment, hospitalization, convalescence care, dental and nursing care, physical, occupational or speech therapy, medical supplies and drugs. The Federal Government also provides for the administrative cost, including expenditure on vocational guidance and placement. During the year 1949 about 58,000 disabled men and women were rehabilitated and placed in suitable jobs at a cost of 30 million dollars.

General medical care for the needy

Before the passage of the Security Act in the year 1936 the Federal Government had only short programmes in the field of medical care for the needy. The local communities took most of the credit for these services. Now medical care is more closely integrated into the federal security programmes. Federal grants-in-aid are distributed through state agencies to provide medical care to recipients of public assistance in local jurisdictions. The Social Security Act requires that federal funds for public assistance be paid directly to the client in a lump sum, without limitation as to the purpose for which the money is required. This prevents the state and local agencies from using federal funds to purchase medical care direct from the persons or agency supplying the service. As a result, the provision of medical care for public assistance clients in many states is limited to the inclusion in the assistance payment of small amounts which the client is expected but not required to use for medical care. It is considered that the direct provision of medical services is far superior to the provision of funds to the client for this purpose. Since the enactment of Public Law 734 in 1950 the ban on use of public assistance funds for purposes of purchase of medical care has been lifted, thus enabling the welfare agencies to develop service programmes which direct payments to the providers of medical care. The medical care extended to the public in different states is not the same. Some states have an organised programme only in their cities; but none beyond their city-limits, except in a few stray instances.

About 5 to 6 million persons (4 per cent of the population) of the country receive medical care at public expense. In some of the wealthier states medical care and hospital services are generally provided to the recipients of public assistance. With a view to rendering medical aid to the poor, the government either conducts its own hospitals or alternatively purchases medical care required for the poor in the absence of the government-owned hospitals, from non-governmental agencies. Local governments and states hospitals, from non-governmental agencies. Local governments and states offer 122,000 general hospital beds, and the non-governmental agencies contribute 349,000 beds. The Public Health departments also have a medical care programme sponsored by them, consisting of : (1) medical and hospital care ; (2) dental care ; and (3) nursing care, for the indigent, medically indigent people, and the poor. In the past health departments mainly functioned towards control of communicable diseases, *viz.*, typhoid, small-pox, diphtheria, plague, whooping cough, etc., and in course of time the incidence of epidemic diseases dropped down at a very fast rate on account of improvement in the educational and general health standards. The health departments could therefore, well afford to shift their main strength and attention from mere epidemic control work to a wider range of services including mass screening for tuberculosis, clinics for cancer detection, diabetes, anaemia, and allied diseases. The immunisation programme conducted by the P.H.S. is admirable. In the year 1948 the immunisations achieved consisted of 1·4 million vaccinations, and 1·5 million diphtheria toxoid inoculations.

Medical research :—Medical research work is considered to be one of the vital functions of the departments of army, navy, and public health services. Some of the outstanding discoveries in different sciences are to be attributed to the officers of these departments. The marine hospital had a hygiene laboratory as early as 1901 and almost simultaneously a volume of research began to flow from this centre, then a very small unit, but now expanded almost to an unimaginable size and scope known as "National Institute of Health"—the largest research centre in the world. The federal government extended the field of research still further, in recent years, through grants of large sums of money to their universities and medical schools. The problem of the United States of America today is not merely the control of epidemic conditions, since they have almost ceased to exist due to the most elaborate and scientific methods of control developed and practised in the past. The average span of human life has increased significantly, due to the elimination of the common health hazards, and the health services have now focussed their attention on eliminating problems which somehow remained unexplored in the past, *viz.*, the problems of old age, chronic diseases, cancer, heart and mental disorders.

My grateful thanks are due to Dr. G. L. Sharma, M.D., Dean, Medical College and Hospital, Nagpur, M.P. for his kind permission to publish this article.

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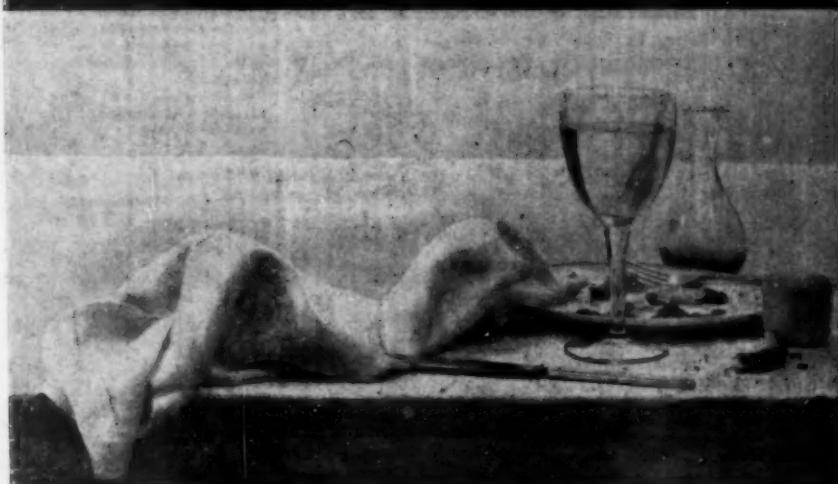
Coronary Thrombosis and its Response to Treatment

The Committee of the American Heart Association recommended in 1948 the use of anticoagulants in the treatment of coronary thrombosis. Many have since reported favourable results with the use of heparin and dicoumarol in thrombo-embolic complications. Dr. Rae Gilchrist, Cardiologist of Edinburgh, gives his latest results using tromexan instead of dicoumarol in some cases. Approximately 43 per cent die from the 4 major complications of acute coronary thrombosis (*viz.*, shock, heart failure, thrombo-embolic incidents, and sudden deaths) during the first six weeks, amongst a group of conservatively treated patients, while the death rate was only 21 per cent in a corresponding group receiving anticoagulants. Deaths from shock are less frequent when anticoagulants were used. Graham *et al* found that 55 of 59 patients with angina pectoris obtained prompt relief of symptoms when given injections of heparin once or twice a week although pain returned when *inert* injections were substituted. The value of anticoagulants in severely ill patients has been established beyond doubt; but "it is difficult to justify their routine use in all cases of coronary thrombosis" is the verdict of the *British Medical Journal*. There must be a conscious selection of cases suitable for anticoagulant therapy. This fact has been brought out by the results obtained by Russek and Zohman in a series of 1047 cases which were treated by them conservatively dividing them into 'good' and 'bad' risks. The good risks included those who, on admission gave no history of previous infection, intractable pain, severe or persistent shock, cardiac enlargement, gallop rhythm, heart failure, and arrhythmias; in the good risks the mortality was only 3 per cent, while 60% died in the group showing one or more of the above signs. In a study of coronary heart disease amongst medical men, by Morris and his collaborators, published in the *British Medical Journal*, Vol. 1, p. 503: 1952, it was reported that the majority of deaths from coronary thrombosis occurred during the first week, that the time of greatest need for therapy was in the first few days of the very first clinical attack and that the death during this period was mostly due to shock and congestive heart failure. Gilchrist therefore, emphasizes the importance of early treatment of heart failure. Though the circulatory changes during cardiogenic shock are still obscure, the hypotension appears to be due to the failure of the viable myocardium and in a severe case he advises the use of digoxin as a cardiac stimulant, inspite of the largely theoretical objections to its use in the presence of a recent infarct. The evil effects of prolonged hypotension, which can itself cause ischaemic changes in the myocardium are no doubt recognized; but there is unfortunately no reliable method of raising the blood pressure. Pressor drugs are still largely in the experimental stage and transfusion has proved a failure in most cases. Further research into the causation and treatment of cardiogenic shock is advocated.—(*Br. Med. Jour.*, 16-8-'52, pp. 351-55 and p. 378).

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¹ Britten, C. J. C. (1950): Practitioner, 164, 458

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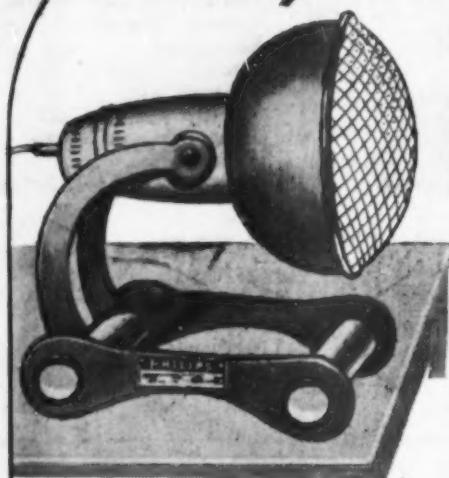
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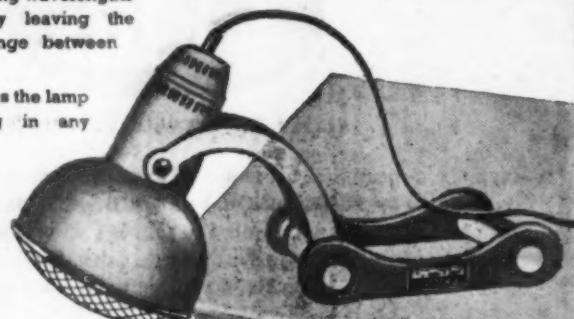
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B. A. NARAYAN, B.Sc., M.B. (cal.),
Regd. Medical Practitioner and Dermatologist,
R. S. Poor Dispensary, Kalasipudi P.O., via Akiridu, W. G. Dt.

LEPROSY is a chronic infectious disease, caused by Hansen's bacillus (*Mycobacterium lepræ*). It is a disease primarily of later childhood, adolescence, and early adult life, though clinical leprosy has been reported in individuals before the age of 2 and after the age of 90.

It is estimated that there are about seven million sufferers from leprosy in the world. Three million of these are within the British Commonwealth, mostly in India and Africa, and of this three million some 300,000 are infective cases in need of prompt treatment, if further infection and spread are to be prevented. But actually proper and adequate treatment is now being given only to about 4,000 of these sufferers.

Though it was first introduced into England about 950 A.D., persons known to be lepers were shunned by the rest of the community since the middle ages. Rigid rules of segregation were enforced in order to prevent the spread of the disease. There was no treatment. The leper was merely put out of sight—and forgotten. And leprosy is no longer a common disease in England.

The reason why people dread leprosy is due to: its disfiguring effects, its persistence (entailing prolonged and intense suffering for many years) and above all the mental anguish involved in facing life as an outcaste from society.

Although the manner in which the infection is transmitted from person to person is still a moot point, leprosy has now come to be considered much less contagious than was once believed. In the past, when no effective treatment was available, the policy of segregation may have been justified as the only way of protecting the rest of the community, but indiscriminate segregation where it is still practised today encourages a victim to hide his condition as long as he can, resulting in other members of the household getting infected. Also the disease thereby progresses too far to benefit by suitable effective treatment administered in time.

Leprosy is slow and insidious in its onset, and may take two different forms: the lepromatous type and the neural type as defined by the International Congress of Leprosy in 1938. The method of treatment, the prognosis, and the degree of infectiveness, vary with the type. Tuberculoid leprosy is non-infective or only very slightly so. Whereas the lepromatous type is infective to children on prolonged contact and also to a small minority of susceptible adults.

The neural (N) Type.—All cases of the "benign" form of leprosy, showing disturbances of a polyneuritic nature (i.e., alterations of

* Specially contributed to **THE ANTIDEPIC**.

peripheral sensation, trophic disturbances, atrophies and paralyses and their sequelæ or macules of a non-lepromatous type (leprides, usually with localized sensory disturbances) or both come under this type. These cases show relative resistance to the infection, have a comparatively better prognosis as regards longevity although some amount of mutilation may take place, and usually react positively to leprolin (lepromin test). The skin lesions are typically but not invariably negative for *M. lepræ*, in bacteriological examinations, though scrapings from the nasal mucosa may be positive; many of these lesions are histologically of a tuberculoid nature. A characteristic feature of tuberculoid leprosy even in its early stages, is that the skin lesions get anæsthetised against light, tactile and thermal sensations. The lesions show well-demarcated edges, and partial pigmentation, and the peripheral nerves near the lesions may be thickened. Bacteriological examination of lesion tissues shows no bacilli though typical tuberculoid changes in the dermis of the affected regions are found in pathological examinations.

Lepromatous (L) Type.—All cases of the "malignant" form of leprosy, relatively non-resistant and of poor prognosis, usually negative to leprolin (lepromin test), exhibit lepromatous lesions of the skin and other organs, especially the nerve trunks. Bacteriological examination usually reveals numerous bacilli. Disturbances of a polyneuritic nature may or may not be present; they are usually absent in the earlier stages but occur in the later stages of the primarily lepromatous cases, and are often also found in cases arising secondarily from the neural form. The two types are often liable to be confused with each other, if proper diagnostic methods are not employed. On careful examination, the lepromatous type may appear in its early stages as a dull flush on the ear-lobes, cheek or other portions of the body. There is no anaesthesia. The edges of the lesions as they develop are ill-defined, and merge in the surrounding skin; the lesions may spread until a large area of the body has become involved. Microscopic examination reveals the presence of *M. lepræ* in large numbers. Nodules containing numerous bacilli, (as many as 7,000 million per sq. cm. of tissue) may appear on the forearms, trunk, and face.

In the prognosis of a particular case of leprosy, use is made of the lepromin test which, in its modern form, involves the use of a standard refined lepromin obtained from specially treated nodules. To carry out the test, one drop of the lepromin is injected intra-dermally. The appearance of a red inflamed weal about one or two inches in diameter 48 hours later indicates a positive reaction; this means that the patient has a high natural resistance to the disease and is likely to respond well to treatment. A negative response means that the patient's natural resistance is low and the treatment will have to be more protracted and should be carefully controlled. Tuberculoid cases usually give a positive reaction and

lepromatous cases a negative reaction. The different types of leprosy which are commonly prevalent in our parts are illustrated in the following photographs of cases still under treatment.



(1)



(1)



(2)

Photograph 2.— Neural type of leprosy in a Mahandra boy J. C. A. of Bhimavaram, aged 24 years, who has been suffering for 18 years, married, but no children. Both the ears, and nose are swollen and distorted, and there are nodules on the forearm, fingers and feet; lesions are present on the wrists of both the arms and white spots (leucoderma?) on the chests and knees.



(2)

The neural type of leprosy may be anaesthetic or macular. In the former, there is evidence of involvement of the nerve trunks only (polyneuritic changes and sequelæ without macular skin lesions); while in the latter the lesions may consist only of flat maculae or of raised tuberculoid macular patches in some cases. The neural type usually follows a long and chronic course. The digits of the hands and feet suffer distortion and degeneration. Ulcers on the hands and feet are common. Areas of anaesthesia

may be extensive. The disease usually becomes dormant, or undergoes remission at certain periods.



(3)



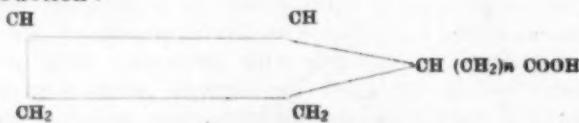
130

Photograph 3.—Tuberculous leprosy in a shoemaker K. V. of Bhimavaram who has been suffering for 20 years. The lesions have well demarcated edges and show partial pigmentation. The enlargement of the breasts is a fairly common feature in advanced cases of leprosy.

The lepromatous type is usually malignant in its behaviour. The mouth and pharynx often suffer extensive mutilation; the eyes are invaded resulting in blindness, and the viscera may also be involved.

Infectiveness.—Individual resistance varies greatly; close and prolonged personal contact is usually necessary for the transmission of the infective agent. Contact during infancy is more liable to result in infection than in later life. Many individuals are practically immune to leprosy, hence the susceptibility of man to the disease varies very widely.

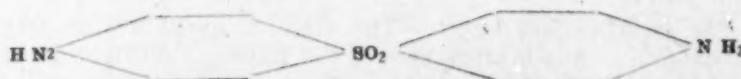
TREATMENT.—For many centuries fixed oils obtained from certain trees of the natural order Flacourtiaceæ have been used empirically in the treatment of leprosy. Those used most are: chaulmoogra oil and *hydnocarpus* oil; but as these are solid or highly viscous they do not readily lend themselves to therapeutic use in their natural state. Research work carried out during many years in various research laboratories in collaboration with clinical workers in the field, has shown that the pharmacological properties of the oils depend on the presence of a particular fatty acid with the following construction :



(In chaulmoogric acid n is 12, in hydnocarpic acid n is 10). In the natural oils the acids are combined as glycerides, but modern treatment makes use of preparations consisting of a selected fraction.

of the esterified acids in a form that is well tolerated. The addition of 4 per cent. of creosote minimises local pain and irritation.

The newer drugs :—A new era in the drug treatment of leprosy began with the discovery in 1943 that drugs of the sulphone group were active against acid-fast bacteria. The parent substance of the group is 4:4'Diamino-diphenyl-sulphone :—



Diaminodiphenylsulphone was first synthesised in 1908 but it was not until 1937 that its pharmacological properties were investigated. It was found to have a remarkably antibacterial activity but although it became well established in veterinary medicine early trials on human beings were quickly abandoned because the compounds appeared to be dangerously toxic. At present several sulphone drug preparations have been put on the market by different manufacturers under different trade names e.g., promin, diamidin, diasone, sulphetrone, cryosulphone, neustab, novotrone, diphone, soluphone, and solfone.

Technique of administration :—A dose of 200 mg. a day should not be exceeded. The patient takes the drug for six days, and has one day's rest, or takes it continuously for 4 weeks and then has 1 week's rest. As the absorption of the drug depends on various factors when given orally, the method of choice is to administer it by the intramuscular route. Promin is used solely for intravenous administration.

Precautions during treatment :—The diet, general care and freedom from secondary infections, should all be carefully adjusted and controlled. As these drugs have got a general depressant action on the haemogenic function of the bone marrow, the blood should be frequently examined for haemoglobin and total red blood cells; the urine and blood concentration of sulphone should also be tested frequently.

Reaction :—On the appearance of fever or the appearance of inflammatory nodes, the drug should be discontinued for a short time, also when the haemoglobin percentage goes below 70% and haematinics and restoratives such as iron preparations, B. complex, liver extract and vitamin C etc., should be given until the normal haemogram is restored.

Sulphones are readily absorbed and slowly excreted. They should be continued for a long time, taking particular care to detect the earliest sign of intolerance. The results will then be very encouraging.

Therapeutic response :—Within two weeks of starting the treatment the patient usually feels some improvement. After 6 months'

treatment remarkably good results are manifest. A week's rest after treatment for three weeks in ordinary cases and 2 weeks' rest after 6 to 8 weeks' treatment in bad cases, should be the rule. The drug is excreted slowly, concentrations of the drug are manifested in the skin, mucous membrane and in the eyes. Best results have been achieved when the drug had been continued over a period of four years.

The social welfare aspect :—The aims of social welfare service are three-fold :—non-medical care of the patient in the institution, care of his relatives and interests outside the institution and care of patients not isolated in an institution.

The patient in the leprosarium :—The social welfare service should care for the patient's spiritual, mental and physical well-being. The patient enters or is put into an institution not only for his own benefit but also in order to protect the community from infection. He thus helps society and is therefore, entitled to be treated well by society, when he gets better. Social welfare services should cater to the needs of the patient's education, occupation, recreation and his spiritual uplift.

(1) *Education* :—Schools are necessary for the children, and illiterate adults can be taught to read by one of the modern simplified methods. Educated patients can act as teachers ; the educational department should provide suitable and adequate equipment. Vocational training should be developed and such trades and cottage industries taught as building, carpentry, masonry, metal work, leather work, weaving, tailoring, basket-making, manufacture of locally grown agricultural products, etc. Practical training should be given to all patients in both general and special hygiene. Cleanliness of body, clothes, dwelling places and their surroundings should be taught both by precept and daily practice. The patient should be made wise about the causes of leprosy, its nature and the methods of treatment and prophylaxis. He is more likely to follow the rules intelligently than the untaught scot-free leper ; when he recovers and returns home he will be a missionary of hygiene and leprosy control.

(2) *Occupation* :—Doomed to remain for years, it may be for the remainder of his life, in a leprosarium, how is the patient to spend his time ? Only occasionally he requires hospitalisation, and his medical treatment takes up only a short time of the day. Patients are of different sexes, ages, trades and occupations ; some have been accustomed to sedentary, others to hard physical work ; some are able-bodied ; others are weakened or crippled by the disease. Still all of them should have something to do, suited to their capacity and general condition. Communal drill and physical jerks have been found to be of great value, as they encourage regularity and help to develop the physique, and also prevent or minimise deformities.

Occupational therapy is an important item in treatment ; when wisely planned it benefits the patient in many ways : thus, it enables him to maintain his self respect, it prevents him from brooding over his ailment ; it keeps him fit and thereby renders medicinal treatment easier, better tolerated and more effective ; finally it helps to prevent serious deformities like the claw hand etc., which are otherwise very liable to occur.

(3) *Recreation* :—Patients should be encouraged to organise their own games and recreations. Music concerts and dramas encourage the creative instinct and please the spectators and the actors. Concerts, and cinema shows, by outside agencies at frequent interval will be of great aesthetic and curative value to nervous persons. These will incidentally help the suffering patients to improve their own efforts at providing entertainments and recreations. Open air theatres are best suited for patients in leprosaria, though provision for indoor performances during inclement weather should be made where possible. Libraries should be provided with a good selection of books and periodicals.

(4) *Spiritual* :—There are some obvious reasons for the need of a spiritual background in a leprosarium : (a) the majority of the patients suffer from chronic mental depression at the incessant thought of their ailment, they are also conscious of the fact that they are abhorred and loathed even by their relatives and friends ; (b) they have lived in new surroundings away from their homes and occupations and from all that they prized in life. All these disquieting factors require to be composed in order to help the patients to become cheerful and contented. They should be encouraged to have a new outlook and purpose in life and an assurance and courage to face the future with a light and blithe heart.

Cerebral Manifestations of Acute Myocardial Infarction.

Cole and Sugarman of the Lebanon Hospital, Los Angeles basing their findings on a careful study of several cases, emphasize the fact that cerebral manifestations may be the predominant symptomatology of acute myocardial infarction. They have cited six cases in great detail. Syncope, convulsions, coma, or hemiplegia may be the only presenting symptoms of acute myocardial infarction. In the six cases presented, central nervous system symptoms so dominated the clinical picture that the brain was suspected as the seat of the pathological process, and the cardiac accident initially was overlooked. No evidence of cerebral thrombosis, embolus, or haemorrhage was found at autopsy. They attempt to differentiate the picture of acute myocardial infarction with predominantly central nervous system symptoms from the combined acute vascular lesions of the brain and heart.—(Am. J. Med. Sci., 223, 1, 1952).

TREATMENT OF BRONCHITIS.*

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THERE has so far been no specific drug which can *cure* bronchitis.

Even the "wonder drugs" of today have not proved very useful. Cough remedies and cough syrups of various descriptions and makes still rule the day and are in great demand by the public although none of them give any real or lasting benefit.

This state of affairs, to our mind is largely the result of a want of proper understanding of the correct pathology of the disease and of the mode of action and proper dosage of the various drugs that are used in the treatment of bronchitis. We therefore, undertook this 'pilot' study in order to find, if possible, a rational and sensible approach to the effective treatment of the disease.

Bronchitis may be either : (a) productive—useful, adequate, or beneficial, or (b) unproductive—useless tussal insufficiency. A productive cough brings out the product of inflammation, foreign bodies if any, or a plug of mucus from the respiratory tract.

Bronchitis is really the successful drainage of the secretions from the inflamed bronchi, under the effect of coughing. In unproductive or tussal insufficiency, the sputum is so thick that little or none of it is expectorated even under the strain and efforts of coughing.

One of the most interesting causes of bronchitis is "Allergy" and the terms "Allergic Bronchitis" and "Asthmatic Bronchitis" have become familiar. They are of two types, *viz.* : (1) the reversible and (2) the irreversible types.

In the reversible type tissue changes are induced by antigens, like pollen, foods and sera and are characterised by oedema, spasm of the smooth muscles and stimulation of the mucous glands. Only the conducting portion of the lungs is affected in this condition. In the irreversible type tissue changes are induced by antigens, like bacteria and their end-products, sera or drugs, resulting in the death of the cells and damage to the vascular tissues.

Fog, damp and cold are the most common agents that readily affect the delicate mucous membrane of the bronchial tree, which becomes oedematous and if the oedema extends further, the peri-bronchial tissues are also affected; the openings of the secretory glands are nearly obliterated, interfering with normal ciliary movements. No consistent or specific bacterial infection to account for

* Specially contributed to THE ANTISEPTIC.

the disease has so far been established, though micrococcus catarhalis, staphylococci and streptococci as well as pneumococci are all found in the bronchial secretions. In the absence of any of the above mentioned causes, a virus infection is usually suspected. The cough is dry and of a hacking nature in the acute stage of the disease. This is due to congestion of the mucous membrane and spasm of the muscular tissues. Breathing becomes difficult, slight pyrexia is usually present with general malaise and distress. Later on, when the oedema subsides, the thick mucous secretion becomes liquefied, the sputum becomes more copious and easy of expectoration. This is the second or the final stage of bronchitis. The pathological changes may affect any part of the bronchial tree: from the larynx to the bronchioles. Tracheitis, bronchitis and bronchiolitis are synonymous terms, but are used to denote the extent to which the disease has progressed.

There are four main factors to be considered in the treatment of bronchitis *viz.* : (1) The relief of congestion and reduction of inflammation of the mucous membrane; (2) the relief of the spasms of the bronchial musculature; (3) the liquefaction and removal of the mucus or mucopus, from the lumen of the bronchi; and (4) the prevention of complications.

The relief of congestion and inflammation.—The time-honoured traditional treatment for this condition is by administering the "stimulant cough mixture" which is believed to stimulate cough, promote secretion, and also lubricate and soothen the inflamed bronchial mucous membrane. This statement is based at best on conjecture, and not on facts ascertained by accurate scientific methods, using proper and suitable controls.

The common drugs used in making up this mixture are ammonium chloride, ammonium carbonate and ipecacuanha. The hospital stock mixture called "Expectorant cough mixture No. 3" is of the following composition :—

B Ammonium carbonate	... gr. v
Tincture scilla	... fl. v
Vinum Ipecacuanha	... fl. x
Spt. aetheris nitrosi	... fl. xxx
Aqua ad. q.s.	... 3 i

Sig. Mixture to be given three or four times a day.

Ammonium chloride is a saline expectorant, soluble in water and prescribed in acid mixtur, as it loses its potency in the presence of the alkalies. The useful dose is 5 grains every two hours or every hour if necessary. In how many instances, are such frequent doses known to have been prescribed or administered?

Ammonium carbonate.—"If concentrated or given in a large dose, both the carbonate and bi-carbonate, cause gastric irritation leading to nausea and vomiting. Doses not sufficient to cause vomiting, stimulate the bronchial secretion reflexly through the vagal

mechanism and are therefore, used as expectorants in many kinds of sub-acute and chronic lung diseases." (Majumdar)

Ipecacuanha.—Perry and Boyd pointed out that ipecacuanha is capable of increasing the secretion of glands of the bronchi. The increased secretion by diluting the viscid inflammatory product assists in the dislodgement and removal of it from the respiratory passages. The emetine and saponin contents of ipecacuanha are believed to be responsible for its therapeutic influence. Bash and his collaborators who studied the action of ipecacuanha recorded that the viscosity of the mucus was lowered but its pH was not influenced. There was a pronounced increase in some patients while in others no change or decrease was noted. Pick and Wasicky thought that the expectoration caused by ipecacuanha was mostly due to the relaxation of the smooth muscles of the bronchi.

Ipecacuanha has no direct action on the bronchial membrane and should be given in toxic or sub-emetic doses to be of any real value. It acts, like the salts of ammonia, through the vagus supplying the stomach. Ammonium salts are powerful gastric irritants and are liable to do harm, particularly in cases of gastritis and to persons with gastro-duodenal ulcers. In patients in whom vagotomy has been performed for some condition or other and the nerve supply has been cut off, the salts of ammonia and preparations of ipecacuanha will have absolutely no effect. Are we justified in carrying out the "scorched earth policy", *i.e.*, try to save the lungs at the expense of the stomach? To what extent will the small quantities of the ingredients in the so called stimulant mixture help in combating the bronchial condition?

Relief of bronchospasms and oedema.—The parasympathetic nerves supply the bronchial musculature through the vagus nerve. Any drug that could counteract or antagonise the action of the parasympathetic system should relax them. What are the drugs in our pharmacopoeia that can produce this effect? Out of a large number only three are being largely used, *viz.*, belladonna codeine and ephedrine.

Belladonna.—The active principle is atropine. Belladonna is a powerful anti-spasmodic and has a tendency to dry up secretions in the body as well as in the bronchial mucous membrane; it is usually prescribed in combination with codeine, a very useful pill being Ext. belladonna viride $\frac{1}{4}$ grain with codeine phosphas $\frac{1}{2}$ grain.

Morphia, codeine and its derivatives.—These are used in cases of tussal insufficiency where there is no thick mucus to be expectorated. Codeine, either in the form of syrup or a pill, is frequently used for this purpose. Syrup codeine phos, B.P.C., contains $\frac{1}{4}$ grain of codeine in one drachm and is widely used. The adult dose should be two drachms given three times a day, for several days. Doses smaller than one drachm are ineffective.

Morphia is restricted to those cases of (1) aortic aneurysm, pressing on the bronchi or trachea ; (2) inoperable tumours of the lungs or mediastinum ; and (3) certain cases of cardiac decompensation failure with irritable cough. Morphia is a powerful depressant of the respiratory centre. It diminishes the muscular tone of the striated muscles including the diaphragm ; inhibits the action of the glands of the bronchi preventing the normal excretion of mucus. It has a tendency to dry up the mucus membrane making the cough more distressing and irritating.

The excessive use of codeine is to be avoided. Morphia, except in the conditions noted above, is prohibited. Giving codeine and belladonna over and above what is absolutely essential is illogical and even dangerous. Suppression of cough is to prevent the normal excretion of the mucus ; and any accumulation of the mucus in the bronchioles is fraught with danger. It may provoke or help the mobilisation of active pathogenic bacteria, leading perhaps to serious consequences.

Liquefaction of mucus.—Christie rightly remarks “ the use of an expectorant or cough mixture to influence the secretion of the bronchial glands, is very much hallowed by tradition and a wide, or even wild, variety of drugs have been used.... Potassium iodide is excreted partially by the bronchial mucous glands and in passing through them stimulates secretion. *This certainly occurs in patients hypersensitive to iodide, but whether there is any such action in normal individuals, is doubtful.*”

The experimental observations of Taft and Levin show that potassium iodide is excreted through the bronchial mucosa in 15 to 25 minutes whether administered orally or intravenously. Bash, Holinger and Poncher noted that after the administration of potassium iodide the viscosity and the pH of sputum were lowered. Potassium iodide is administered in the form of enteric coated tablets of 7½ grains to 15 grains each or in solution in syrups used for flavouring or as a saturated watery solution, three or four times a day. Barach is of opinion that potassium iodide is one of the most valuable drugs to combat intractable bronchial spasm and inadequate expectoration of viscid mucus. The ingestion of 4 or 5 c.c. of a saturated solution daily, in divided doses, for four days, followed by one or two c.c. over an indefinite period causes the secretion from the bronchi to become thinner and lessens the possibility of the formation of mucus plugs in the smaller bronchi.

Our centuries-old treatment of bronchitis by “steam inhalation” may still be relied upon. Its use has been clinically proved very useful particularly in the case of children. Bash, Holinger and Poucher carried out careful investigations on the effect of the steam or moisture inhaled on the physical and chemical properties of the sputum and noted that after steam inhalation, the viscosity

was greatly reduced and the dried residue and the total nitrogen content had been markedly reduced. The addition of volatile oils to the steam increases the secretion of the glands of the bronchial system and stimulates bronchial peristalsis and ciliary movements.

Relief of mucus.—The most valuable and readily available measure for the relief of mucus is 'hydration'. Water is the best of all expectorants—much better than the "stimulant cough mixture" of doubtful utility. This simple but effective measure of relief has not however, found a place in text-books. Hydration liquefies the mucus, prevents inspissation and thickening that lead to a choking and obstruction of the bronchi. Warm drinks are very helpful. To quote Feingold "it may seem paradoxical to emphasise the importance of giving large quantities of fluids 1,000 to 2,000 c.c., in 24 hours—in a disease in which tissue oedema plays such an important role in the production of the symptoms, but clinical experience has consistently demonstrated, often with dramatic response in a few hours, the benefit of such therapy."

A 5% dextrose solution in water is most valuable when given intravenously. Saline solutions should *not* be used as there is already sodium chloride retention in the system. The use of steam inhalation, preferably medicated with Tr. Benzoin Co. or a volatile oil *e.g.* eucalyptus oil or a combination of these will greatly help in the removal of mucus from the bronchi.

Relief of oedema and bronchospasms.—There are quite a large number of sympathomimetic drugs for the treatment of the allergic bronchitis; epinephrine and ephedrine which have the properties of vasoconstriction and muscular relaxation, are the two most commonly used of these drugs.

Drugs like Isopropylarterenol (Isuprel), Isopropyl-epinephrine (Aludrine) and Isopropyl-nor-Adrenalin (Isoprenaline) are powerful broncho-dilators. They have no vasoconstrictor-action and cannot therefore, efficiently control the oedema of allergic bronchitis.

Epinephrine is a most rapid and powerful broncho-dilator and vaso-constrictor. It should prove of great use in the active stages of allergic bronchitis, but owing to the short duration of its action, its use is limited to acute asthmatic episodes.

The antihistamines have a tendency to constrict the blood-vessels and dilate the bronchioles. Despite these desirable properties, many clinicians use them very sparingly, because the results obtained with them have been disappointing. They should be used cautiously, for owing to their atropine-like action they dry the mucous secretion and aggravate the cough.

Xanthine drugs like alkaloidal caffeine, aminophylline and theophylline, owe their efficacy to their broncho-dilator action. They have a vaso-constrictor-action as well, but the peripheral vaso-dilator action is the more predominant one.

Rectal suppositories of Theophylline-ethylene-diamine (Aminophylline) are very useful in the case of infants on certain occasions. If the suppository is not available, one can safely use a 10 c.c. vial containing 0.25 gm of aminophylline diluted with 20 cc. of water and give it as a "rectal cocktail."

For children, a combination of equal parts of a solution of 1:100 or 1:200 of Neo-synephrine and 1:100 of Isuprel in 10% glycerine could be used by nebulization. We have used with good results the nasal solution of Isopropyl-nor-adrenalin (Isoprenaline) diluted to suit the needs and ages of the patients. Antistine-privine solution is another combination useful for both children and adults. The use of bronchodilators in powder form or in "dust" is risky as severe and alarming palpitation of the heart has been found to result.

When antihistaminics are given orally the least toxic ones are to be preferred. A few patients derive some benefit by the use of Pyribenzamine by day and Benadryl by night. But none of these antihistaminics have given appreciable relief.

Ephedrine.—By virtue of being a stimulant of the sympathetic nervous system, it causes relaxation of the bronchial muscles and is used in doses of 1/4 to 1/2 grain three or four times a day. It may be used instead of atropine or belladonna. This drug should not however, be repeated too frequently as the duration of its effect diminishes with each successive dose. If given in excess, it produces unpleasant side-effects like jittery shakes, wakefulness and nervousness. This drug should be used very cautiously in cases of hyperpiesia, as it has a tendency to raise the blood-pressure, especially in the aged persons.

Other forms of treatment.—Mustard poultice over the chest was the old time practice. This was followed by Antiphlogistine. One fails to understand the rationale behind the grand idea of applying external heat to control a disease in an organ placed within a bony thorax and inches away from the seat of its application. Perhaps there is better sense in the "hot foot-bath" and a stiff dose of brandy together with 5 or 10 grains of aspirin than in this thermotherapy. It has already been pointed out *supra* that there is no specific organism that would account for bronchitis and none of the organisms that are usually present in the secretion, may be responsible for the disease. Strange to say, auto-vaccines were prepared and used. Many extolled them to the skies while others unequivocally condemned them as useless. Sulphonamides were once very popular but have now been discarded. Penicillin, in all its forms next came to be used, even as a snuff and the results were not considered uniformly good. It is our experience that penicillin and sulphonamides, inspite of their drawbacks, benefit

certain cases and good results are obtained, particularly when complications set in.

Penicillin is best given by inhalation, 100,000 units in one charge, as powder or in solution, the treatment being carried out every three or four hours. One such charge is usually sufficient for three or four treatments.

Carbon dioxide.—On the basis of the observations of Henderson, Banyai administered carbon dioxide to many patients suffering from bronchitis, and found it very useful in all cases where there was tussal insufficiency and hacking cough. He says "the benefits resulting from its use are noticeable subjectively and objectively :—(1) Spells of strenuous exhausting cough are prevented, and rest is thereby secured for the patient and particularly for his lungs ; (2) an unproductive cough is transformed into a useful one ; (3) directly after inhalation the amount of expectorated sputum is increased and its character changes from a heavy, thick and tenacious type into a thinner, serous and more watery kind ; and (4) the use of expectorant drugs and narcotics could be reduced."

The effectiveness of carbon dioxide is manifestly due to the following factors :—(1) Being a powerful respiratory stimulant it induces increased inspiratory movements of the diaphragm and the chest wall, which in turn causes a stretching and dilatation of the bronchial tubes ; (2) it stimulates the myoelastic structures of the lungs and causes powerful peristaltic movements of the bronchi ; and (3) it liquefies mucopurulent inflammatory exudate that stagnates in the bronchial tract. This treatment cannot however, be carried out in most stations for want of adequate facilities.

Discussion.—Since bronchitis may be produced by several causes the physician should first ascertain and then treat the cause, which may be a distant irritation, e.g., cardiac, pleural, abdominal, diaphragmatic, pharyngeal, aural, or tubercular and sub-diaphragmatic inflammation. It may also be due to foreign bodies, intestinal worms, thoracic aneurysms and eosinophilia of the lungs.

Antihistaminics and drugs of the xanthine group, may be of value in bronchitis due to allergic irritation. A few atomised sprays of any antihistaminic solution like Antistine, Privine, Neosynephrine, 1 : 100 or 1 : 200 or Isoprenaline, are useful. Where none of the above are readily available, a 2% aqueous solution of ephedrine will act just as well. Care should be taken not to give drugs of the phenobarbital group, simultaneously with the antihistamines, as such medication is reported to have produced disastrous results.

Morphia is effective in bronchitis of cardiac origin and should be given with caution and in appropriate doses only. The cough

and dyspnoea due to failing compensation of the heart could best be treated with digitalis or other specific drugs.

In ordinary bronchitis due to cold and damp with no definite pathology, the treatment should be directed towards (1) the reduction of the inflammation of the bronchi; (2) the relief bronchospasms; and (3) the increase of the glandular secretion of the bronchi.

In the first stage of the disease, codeine, atropine and ephedrine, are indicated. The traditional "stimulant cough mixture" is absolutely without effect in this stage of the disease. Hydration and steam inhalations with volatile oils or/and Tinct. Benzoin Co. are very useful. (Menthol 3 grains in compound Tincture of Benzoin 60 minims, added to a pint of steaming but *not* boiling water). Turpentine stypes three or four times a day, to the chest—a time-honoured treatment—is effective particularly in children, who cannot or will not inhale the medicated steam.

In the 2nd stage of the disease, when liquefaction of the mucus is desired, 7½ to 15 grains potassium iodide three or four times a day in the form of a syrup or as saturated solution or as enteric coated tablets, will be very helpful. The ammonium salt, more especially, ammonium chloride (5 grains) every two hours will be effective. Every other expectorant has its own limitations. Hydration and steam inhalation will be helpful even in this stage and may be continued for a prolonged period.

Inhalation of carbon dioxide is a new advance in treatment and should prove very useful. But unfortunately its use will be limited to only the rich who could afford such treatment in a large hospital. Most of our hospitals are not provided with carbon dioxide and the necessary B.L.B. inhalers.

Of course, adequate bed-rest and nutritious diet are essential. "Feed the cold and starve the fever" is an age-old adage, which is not without some significance. When there is a slight temperature and generalised pain over the body, a small dose of aspirin will be effective; when complications are apprehended or have set in, penicillin and sulphonamides are promptly indicated.

Quite often a combined therapy is used: combinations of several expectorants, and sedatives are usually given at the same time; for instance, Ammonium carbonate or chloride, Ipecacuanha, Tolu, Tr. Camphor Co. or Syrup of Codeine and Potassium Iodide, are prescribed at the same time. This sort of "Molotov's Cocktail" is to be condemned as it is illogical, irrational and wasteful if not also harmful. ("Molotov's Cocktail" is a medley contraption of fuse-operated petrol bottle-bombs, incendiary and destructive in nature, which is hurled over the enemy's camp, for multiple destructive purposes!).

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Bowel Infections in the Tropics

Dr. Adams of Liverpool opening a symposium on the chemotherapy of tropical diseases, before the section of Tropical Medicine of the Joint Session of the British and Irish Medical Associations, held on 11-7-1952, at Dublin said:—"In bacillary dysentery, British practice had been to prefer one of the unabsorbable sulphonamides, though the Americans often used sulphadiazine. The correction of dehydration and the alkalinization of the urine were important when using absorbable sulphonamides, as with these there was the danger of crystalluria and renal blockage. In cholera, vibrios multiply so rapidly that chemotherapy would be too late to be useful. Concerning amoebic dysentery, it was unwarrantable to ascribe to *E. histolytica* bowel infection a limitless range of indeterminate symptoms remote from the abdomen. For bringing an acute attack under control, emetine hydrochloride given for a few days intramuscularly was still unequalled. To eradicate basic intestinal infections, a combination of drugs was effective in most cases. In a series of cases treated by Dr. Adams, he found aureomycin cured 23 out of 27 infections and terramycin cured 46 out of 49. These two were useful additions to the range of amoebicidal drugs; their main value was their capacity, when given with the older amoebicides, to eradicate the occasional refractory infection. Their indiscriminate use in ordinary cases of amoebiasis was not recommended." In the discussion that followed Dr. Adams's conclusions found unanimous support. Prof. H. E. Shortt of the London School of Hygiene and Tropical Medicine (a former Director of the King Institute, Guindy) presided. —(*B.M.J.*, 26-7-'52).

Hypopotassemia in Diabetic Patients in Coma

Intractable shock which often follows coma controlled by insulin, is due to lack of contractility of the myocardial fibrils from insufficiency of serum potassium. Bertolini and Scapellato emphasize the importance of serum potassium in regulating muscular contraction and indicate the causal factors of hypopotassemia in the course of diabetic coma. Regression occurs in ECG changes in coma, after the administration of potassium and diabetic coma is also controlled thereby.—(*Gior. Clin. Med.*, 32, 1951: Abst. in *J.A.M.A.*, 21-7-1951).

DIAGNOSIS OF TUBERCULOUS MENINGITIS IN CHILDREN*

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EARLY symptoms of tuberculous meningitis are unreliable and later ones, excluding the terminal ones are suggestive of the diagnosis ; and thus the diagnosis can be either extraordinarily easy or extremely difficult in a given child. Any doubt in this direction has to be explored relentlessly until elimination or confirmation regarding the disease is obtained.

The duration of the illness may be from 6 days to 6 weeks ; and an acute form may supervene on symptoms of intracranial neoplasm due to a tuberculoma.

Children that came under my care in and outside the hospital were seen with one or more of the following :—fever, fits, drowsiness, incessant crying, vomiting, diarrhoea or cough.

The following table summarises the symptoms of tuberculous meningitis :—

Prodromata.—Importance of previous head injury ; measles ; pertussis ; loss of appetite ; irritability and wasting.

STAGE I (Meningo-cortical irritation) : duration 1 week ; heralded by fits ; fever (high). Cerebral type of vomiting. Headache. Rapid pulse becoming slow and irregular. Constipation. 'Hydrocephalic' screaming. Contracted pupils. Restlessness and muscular tremors. Bulging fontanelle with photophobia and a commencing squint.

STAGE II.—(Rising intracranial tension) duration 1 week :—Attitude of flexion ; child lies on the side. Dysphagia. Drowsiness. Constipation, wasting and carinated abdomen. Irregularity of pupils, squint, ptosis and papillœdema. Fits. Pyrexia (lower grade). Slow and irregular pulse and respiration. Head retraction and trachy cerebrale.

STAGE III (Paralysis and coma) duration 1 week :—Drowsiness deepens into coma. Fits and paralysis. Spasms and contraction. Hemiplegia, monoplegia and Weber syndrome. Eyes half open and dilated pupils. "Typhoidal" stage with rapid pulse, diarrhoea, incontinence. Loss of corneal and conjunctival reflexes. Hyperpyrexia heralding death. Choroidal tubercles. Kernig's sign.

Tuberculous meningitis can be a clinical type of acute miliary tuberculosis, rare under 5 months of age, and even with a negative Mantoux test. Constipation, headache (complained by only older children) appreciated by hearing 'screams' and vomiting form a

* Specially contributed to THE ANTISEPTIC.

diagnostic triad described by many writers, but unfortunately do not afford a very valuable basis for diagnosis in my experience as every practitioner knows in South India that the elusive ascariasis can present all the above symptoms. It is honest confession to say that many children with meningeal manifestations due to ascaris infestations have made me think at one time or another of the dreaded tuberculous meningitis.

Lumbar puncture yields cerebrospinal fluid which is characteristic and diagnostically helpful. C.S.F. is under pressure, forms a cob-web coagulum on standing with increase in protein, slight fall in glucose (stressed as the most reliable single finding during recent times) and a definite fall in chlorides (below 650 mgm. %), and with a usual lymphocytic or rarely polymorphonuclear preponderance. B. tuberculosis can often be demonstrated in the centrifugalised C.S.F. and diagnosis can thus be clinched.

My impression is that a meningeal heave, irregular pulse and lowered chloride count in C.S.F. form a reliable tripod of diagnosis.

Tuberculous meningitis has to be differentiated from the following:—1. *Typhoid fever* :—Widal test may be positive up to 1 in 100 even in tubercular meningitis, but agglutination in increasing titres suggests typhoid fever only.

2. *Pneumonias* (especially apical types):—Predominant pulmonary signs and pulse respiration ratio and at least therapeutic response are helpful.

3. *Ascariasis* :—This common condition can simulate tuberculous meningitis so thoroughly that I can recollect many errors in this direction. Lumbar puncture and follow-up will decide the diagnosis. The lowered sugar content in C.S.F. singularly helping in the diagnosis of tuberculous meningitis is a point on which much has to be said. The normal values for sugar in C.S.F. vary and therefore, dependence on a lowered chloride content of C.S.F. is justifiably more in vogue and fairly reliable in the diagnosis of tuberculous meningitis.

4. *Encephalitis* and encephalomyelitis, (polio and mumps included). Lumbar puncture settles the point.

5. *Otitis media* and its complications, intracranial.

6. *Intracranial tumours* :—(Tuberculomata). When a tuberculoma ruptures into the C.S.F. a typical picture of tuberculous meningitis supervenes.

7. *Congenital syphilis* :—Manifestations are generally in the third month. Serum reaction and therapeutic response are aids.

8. *Cerebrospinal meningitis* :—Occurs with marked head retraction. Lumbar puncture helps.

9. *Malaria* specially cerebral malaria. Blood examination and therapeutic benefit from antimarial drugs help.
10. *Pyelitis* :—Urine examination and culture aid.
11. *Subacute bacterial endocarditis* :—Cardiac condition and changing murmurs and emboli are characteristic.
12. *Teething* : indigestion, malnutritional states and scurvy.
13. *Incubation of eruptive fevers* :—Here is a field which may delude the most wary physician. Guarded prognosis and conservative treatment are essential, till the eruption or the lumbar puncture settle the issue. During the incubation of measles in a baby, I have seen suspicions of tuberculous meningitis being raised. Lumbar puncture results also suggested the possibility of tuberculous meningitis ; but measles-rash put the child very safe.

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Chloramphenicol for Pelvic Inflammatory Disease

Stevenson and his co-workers treated with chloromycetin thirty two patients, 15 with pelvic inflammatory disease of the non-puerperal type with pelvic abscess, nine with infected abortion, two with post-partum sepsis, five with subacute salpingitis without pelvic abscess and one with ruptured appendix. The infecting organisms were isolated and found to be chiefly *B. coli*, nonhaemolytic streptococci, and *B. aerogenes*. 29 of the 32 patients showed a mixed infection. *Staphylo-albus* was the offending type in one case, while *beta-haemolytic-streptococci* were isolated from a case of septicæmia following criminal abortion. A total daily dose of 2 gm. in divided doses of half a gram orally every three hours was given for 10 days. 21 of the 32 patients had previously been treated with penicillin, sulphadiazine and/or streptomycin and 16 of these 21 derived absolutely no benefit, three showed poor response, and fairly good response in two. Only three of the 32 patients failed to respond in adequate measure to treatment with chloromycetin.

The clinical response to this antibiotic was manifest in pronounced symptomatic improvement within 48 hours, rapid disappearance of peritonitis and subsequent regression of the tubo-ovarian inflammatory masses ; the patients were able to undergo exploratory laparotomy within a month in the average case. Women who had large pelvic abscesses were treated quite effectively with chloromycetin ; and posterior colpotomy, with drainage of the abscess, was not necessary for a rapid cure, in patients who were treated exclusively with chloromycetin from the very beginning.—(*Am. J. Obst. and Gynaecol.*, 61, pp. 498-514, 1951).

THE VALUE OF ANTIBIOTICS IN TREATMENT*

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ANTIBIOTICS now enjoy a wide reputation, since their advent revolutionised the treatment of many medical and surgical diseases which formerly took a heavy toll of human life. The combined use of chemotherapy and antibiotics has reduced the incidence of respiratory diseases. "The combined death-rate from influenza and pneumonia is only half of that six years ago and one-fourth of that in 1937, when chemotherapy and antibiotics were not known. Diseases like tuberculosis, diarrhoea, enteritis, pneumonia etc., which headed the death-roll forty years ago and offered problems to the patient and the physician, have now lost much of their terror.

* The list of antibiotics is growing rapidly. The extravagant claims made by manufacturing firms have yet to be proved in many cases by repeated trials and tests, before assigning them to their proper places in therapeutics. But some of them have established their usefulness and deserve to be considered more closely.

Penicillin.—Penicillin is the first of the series and its value in therapeutics, medical and surgical is now fairly well established. Infections caused by gram-positive organisms *beta*-hemolytic streptococci, pneumococci, *alpha*-hemolytic streptococci, gonococci and spirochetal infections, gas gangrene, etc. are readily controlled by it. The discovery of procaine penicillin in aqueous suspension or in oil has obviated the necessity of frequent injections. Even with the soluble salts of penicillin it has been found both convenient and effective to increase the dose gradually at each injection. I use frequently 2 or 3 lacs units of penicillin twice daily, even in cases of pneumonia in children with encouraging results.

The use of *caronamide*, a stable crystalline substance which presumably delays the renal excretion of penicillin, along with penicillin has increased the plasma concentration of the antibiotic from 2 to 32 times. A combination of 2 g. each of caronamide and sodium benzoate orally further enhances the plasma penicillin levels. It is however not advisable to use them in genuine cases of renal disease.

The advent of oral penicillin has further facilitated the use of the antibiotic and obviated the necessity for frequent pricks with the needle; but recourse to this route should be had only in milder infections or when the intensity has been alleviated by parenteral administration. The higher doses needed, often as much as five times the parenteral dose, and the cost to the patient are the main draw-backs to its oral use.

* Specially contributed to THE ANTISEPTIC.

The local use of penicillin in general surgical conditions like wounds, boils, abscesses, carbuncles, sinuses, and empyema cavities, in eye conditions and in many staphylococcal and streptococcal skin diseases, has changed the entire outlook and prognosis of these diseases.

Aureomycin.—It has a wider range of activity and is inimical to a variety of both gram-positive and gram-negative bacteria; and protozoal and viral infections. The greatest advantage is its effectiveness when used orally. In cases of vomiting and in comatose conditions or in fulminating infections, the intravenous route is to be preferred as it produces promptly high concentration levels in the blood. Aureomycin has proved beneficial in practically all the infections sensitive to penicillin. Further, virus or virus-like diseases like atypical pneumonia, lymphogranuloma venereum, trachoma, herpes zoster, whooping cough, mumps, virus influenza etc., are amenable to it.

It is still in the experimental stage as far as prophylaxis and treatment of syphilis are concerned and the available reports are somewhat conflicting.

Cases of acute gonorrhœa and epididymitis, especially those resistant to penicillin respond to it. Soft-chanchroid responds to both local and oral administration but the treatment should be continued for 2 to 3 weeks to effect a cure.

I have tried it in whooping cough. If started early, it mitigates the intensity and increases the interval between paroxysms more effectively than any other drug. It has been tried in certain skin infections like dermatitis herpetiformis, pemphigus, erysipelas, boils and carbuncles. It is quite effective in a number of diseases. Genito-urinary infections of mixed bacterial etiology and gram-negative infections of the coli group also yield to aureomycin.

It is being tried in cases of both acute and chronic amoebiasis as it is effective against the cystic as well as the trophozoite forms. The evidence goes to show that the drug is directly amoebicidal. Claims have been advanced by some about its efficacy in sterilizing carriers.

Terramycin.—This is a comparative new-comer into the field of antibiotics. Like aureomycin, it has a wide range of activity against gram-positive and gram-negative bacteria, both aerobic and anaerobic and against certain of the viruses also. Its therapeutic range is more or less the same as that of aureomycin. It can be used locally, orally and intravenously.

Streptomycin and dihydro-streptomycin.—These are also active against gram-positive and gram-negative organisms. Their toxic action in producing cochlear nerve palsy and tendency to bacterial resistance have limited their use. Their main use now is in exudative forms of tuberculosis, preferably in combination with

PAS. The drug has proved in its worth urinary tract infections and also in endocarditis caused by streptococcus faecalis.

Chloromycetin.—This is another poly-target antibiotic with bacteriostatic and bactericidal properties against a wide range of both gram-positive and gram negative organisms, bacillus typhosis and paratyphoid A and B and also viruses. It is effective orally; in infants and children it can be given also rectally. It can be combined with other antibiotics and sulphonamides. It has proved effective in treating acute gonorrhoea and syphilis. Urinary infections, both bacillary and coccal are amenable to its action.

It has however, been most extensively used in the enteric group of fevers. It controls the temperature in 3 to 5 days and the general physical condition improves appreciably. The consensus of opinion favours the view that the drug should be continued for 2 or 3 days after the attainment of normal temperature in order to prevent relapses; smaller doses at longer intervals will do.

The chronic typhoid carrier-state does not seem to be affected at all by chloromycetin but enteritis following enteric fevers responds to it rapidly.

Secondary complications like bronchitis, broncho-pneumonia following measles are readily controlled with this antibiotic. Clinical experience in *pertussis* has been quite favourable. The number and intensity of the paroxysms are reduced regardless of the stage at which the drug is begun.

This antibiotic has been administered in gonococcal infections and in syphilis, but the results so far obtained do not show any special advantages over those obtained with penicillin and aureomycin.

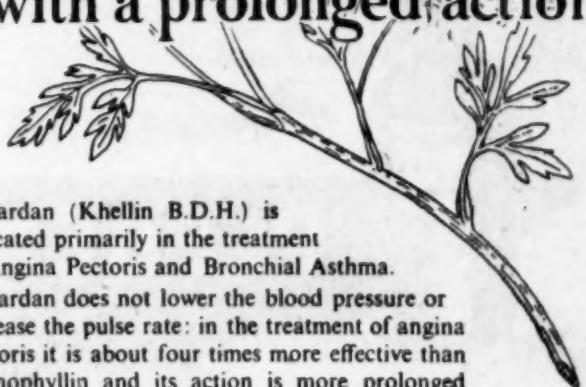
It exerts a favourable influence on trachoma; within 24 hours photophobia and lacrimation are lessened; and corneal involvement is prevented, if the treatment is started early.

Summary.—The therapeutic activities of some of the main antibiotics which have stood the test of time and trial are briefly reviewed. Laboratories of manufacturing firms and biochemists over the whole world are constantly adding to the list. It is unfortunate that with the exception of penicillin and perhaps streptomycin the rest of the antibiotics are much too expensive to be within the reach of the large proportion of our suffering humanity as India is a poor country and the majority of the people cannot afford to buy them. Efforts, are being made by our Union Government with the combined help of the WHO and UNICEF to manufacture Penicillin in India and make it available at cheaper prices. OG also, we hope, will the other antibiotics come to be manufactured in India in course of time and sold at cheaper prices.

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Amer. Heart J., 1949, 37, 531. Brit. Heart J., 1950, 12, 54.

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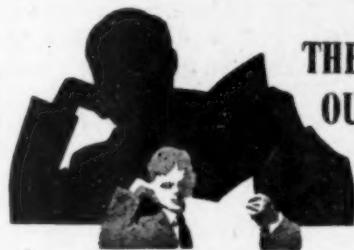
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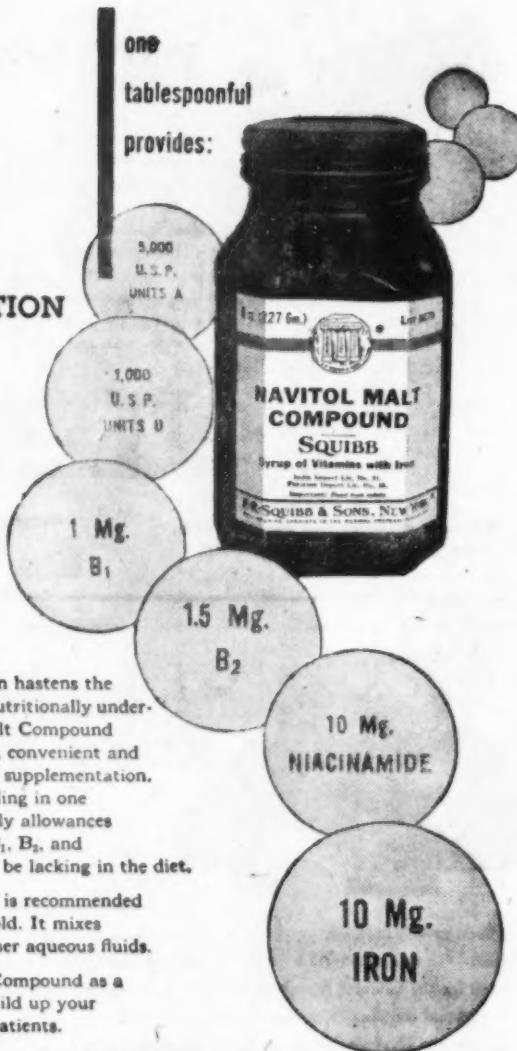
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TWO UNUSUAL CASES OF DEATH FROM ACCIDENTAL INJURY

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MINOR injuries sustained during the process of splitting firewood are not infrequent; but it is rare that injuries inflicted during this act turn out to be serious and rarer still to find them severe enough to cause death on the spot. During the latter half of 1951, two such fatal cases were examined in this department and in view of the unusual method of causation and nature of the injuries, it is considered that brief reports about them will be of interest.

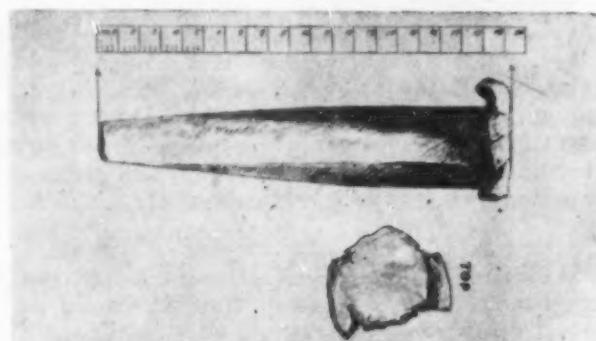
Report of Cases

CASE I.—History :—S., Hindu, male, aged 35, and G., another adult male, were engaged in splitting wood at 4 p.m. on 7-7-'51 in a firewood depot in Poonamallee Road near Aminjikarai, Madras, using an iron chisel and hammer. The chisel about 7 $\frac{1}{2}$ " long, was made entirely of iron, weighing 45 ozs., pointed at one end and almost flat at the circular top, the diameter being about 2 $\frac{3}{8}$ " ; (*Vide photo* on page 796). A piece of iron breaking off from the chisel-head used by G., flew in the direction of S., who was standing at a distance of about 12 feet and pierced his body on the left side of his back. S., had no clothing on his body above the waist and the injury caused profuse bleeding. He was taken at once by G., to a practitioner of indigenous medicine in the neighbourhood who advised the victim to be taken to the Government General Hospital as he was not in a position to remove the foreign body or to control the bleeding. Within ten minutes, and before even a cart could be brought to transport him to the hospital, the victim died having lost in the meanwhile, a large quantity of blood through the wound. The body was sent to this department on 8-7-'51 by the Inspector of Police, Aminjikarai, with a requisition to conduct a *post-mortem* examination. Accordingly the examination was conducted by Dr. P. S. Babu Naidu on the same day.

Autopsy abstract :—The body was that of a fairly well nourished individual 5 feet high. A pair of khaki shorts and a torn piece of red cloth with bloodstains were found on the body. A punctured wound $5/8$ " x $3/8$ " was present on the left side of the back just below the lower border of the 10th rib, about 5" away from the midline. The external wound was directed downwards and inwards and showed lacerated margins. On dissection, the punctured wound was found entering the pleural cavity through the 10th intercostal space, passing through the diaphragm and extending through the

entire thickness of the pulp of the spleen to the middle of the visceral surface and a piece of black metal $1\frac{1}{8}'' \times \frac{3}{4}'' \times \frac{1}{8}''$ was found embedded in its substance. (*See photograph*). The abdominal cavity contained 20 ozs. of blood and the left pleural cavity about 10 ozs. Except for the appearances due to loss of blood, there was nothing pathological in the rest of the viscera.

1. Photo of a sketch of an iron chisel and its irregularly flattened top portion.



2. Photo of the specimen of spleen in Case I showing the site of entry of the iron piece on its diaphragmatic surface.

CASE II. History :—A., Hindu male, aged 30, was engaged at 3 p.m. on 28-9-'51 in splitting firewood by means of a hammer and an iron chisel, similar to the one shown in the sketch, in a depot at Kancheepuram-Sabapathy Mudali Street, Kondithope, Madras, when a piece of iron chipped off from the flattened top of the chisel and entered his left thigh causing severe bleeding. He was taken to the Casualty Department of the Government Stanley Hospital, Madras, at about 4.30 p.m. and after the necessary first-aid, was admitted in the Bryson Ward of the same Hospital. In the casualty room, a gaping incised wound $1'' \times \frac{1}{2}'' \times \frac{1}{2}''$ was noticed in the front of the left thigh at its upper part. The patient was unconscious, gasping for breath and the pulse was almost imperceptible. Coramine, glucose, A.T. serum, A.G.G. serum, oxygen and saline were ordered, and the wound was cleaned and dressed with pressure

bandage. After treating for the collapse under local anaesthesia, at 4.55 p.m., the wound was enlarged, a foreign body consisting of a bit of iron about 2 mm. in thickness was removed from the wound, the femoral artery was ligatured and after controlling the bleeding points, the wound was partially closed. Subsequently, in spite of suitable measures for combating shock and collapse the patient died at about 8.30 p.m. The body was sent by the Police to this Department at 12.30 p.m. on 29.10.'51 for a *post-mortem* examination which was conducted on the morning of the next day by Dr. C. B. Gopalakrishna.

Autopsy abstract :—The body measured 5' 4", weighed 109 lbs. and was that of a well-built person. There was an irregular partially sutured wound over the inner aspect of the left thigh $3\frac{1}{4}$ " x $2\frac{1}{2}$ " the upper end being $3\frac{1}{4}$ " below the Poupart's ligament. On dissection, the femoral artery was found tied in two places and the femoral vein in one place. Other viscera were normal except for the effect of blood-loss.

REMARKS.—It is a common sight in the firewood depots of Madras to see well built muscular individuals, very scantily clothed usually with only a small loin cloth engaged in splitting wood with the aid of hammer and chisel. Examination of these iron chisels would often show the irregularity of their upper surface, several bits having broken off from the edges during gradual daily use (*see sketch*). No mishap however, takes place ordinarily and the workmen continue to earn their living in this way, doing this work for days and months on end. It is a strange coincidence that within the space of four months, two such innocent hardworking men became the unfortunate victims of fatal injuries caused by small fragments originating from their own tools. In one case, it was a co-worker's chisel that shot out the projectile, while in the other, the offending metallic piece was part of his own chisel. Bleeding resulted which was not easily controlled by first aid measures since the spleen and the femoral vessels respectively, were involved in these two cases.

It is interesting to speculate whether these fatal injuries would have resulted if the projectiles had to pass through a layer of clothing. Though climatic conditions and the arduous nature of the work may be partly responsible for the scantiness of the clothing, yet poverty has also to be reckoned with, as a contributing factor. It is sad to reflect, therefore, that poverty expressed in lack of proper clothing should *per se*, have contributed to the gravity of the accident which in its turn, led inevitably to more poverty by snatching away the breadwinner of the family. It is painful also to note that the force of the heavy blow on the chisel by the hefty workman in Case C, should have become the propelling force for the projectile which caused his own destruction.

Another interesting point to speculate on is the assessment of responsibility in these accidents, in relation to the Workmen's

Compensation Act and also about the question of culpability if one is raised in a Court of Law. How far is the employer responsible in such cases where the tools provided by him are not up to the mark in temper and other qualities, where sufficient space is not made available for the workmen to do their work at a safe distance from one another, and where facilities to render 'first aid' in sudden accidents are not even thought of.

Acknowledgements.—My thanks are due to the Superintendent of the Government Stanley Hospital, Madras, for permitting me to extract notes about Case II from his hospital records.

Aureomycin in Acute Gonorrhœa

63 male patients between the ages of 14 and 56 suffering from acute gonorrhœa were treated by Wright *et al.*, with aureomycin. A single capsule containing 500 mg. of aureomycin was given initially and a second dose of 500 mg. six hours later. The clinical follow-up showed that the course of the disease was strikingly uniform in all these 63 patients. Within 24 hours, smears and cultures were negative for gonococci in most cases, and the thick purulent discharge had disappeared completely, though a few patients had a thin watery discharge which was however, free of gonococci. After 48 hours, the urethral discharge had completely disappeared. Sixty patients of the 63, who were fully followed up were cured, i.e., they showed no clinical symptoms and bacteriological smears and cultures were negative. The other three were therapeutic failures. With the dose employed toxic reactions were quite minimal and high urinary levels of the antibiotic were obtained, which persisted for atleast 48 hours in 3 of 4 patients. The results showed that aureomycin is as effective as penicillin in the treatment of acute gonorrhœa. Aureomycin however possesses certain definite advantage over penicillin:—(1) ease of administration; (2) minimal toxicity limited to the gastrointestinal tract; (3) little or no increased drug-resistance of the gonococci (4) beneficial effect in concurrent gram-negative bacterial urinary tract infections often found associated with gonorrhœa, and not amenable to penicillin therapy. Aureomycin should therefore, be considered one of the agents of choice in the treatment of acute gonorrhœa.—(*Urol. and Cut. Rev.*, 55; pp. 203-206 : 1951; abstr. *J.A.M.A.*, 217-1951).

Diet and Appendicitis

From a review of the literature, Van Ouwerkerk gained the impression that acute appendicitis is comparatively frequent and dangerous in Northern Europe, America and Australia. Among native populations in Asia and Africa, but not among Europeans living there, appendicitis is rare. When the natives eat the richer diets of Europeans, then they also have a higher incidence of appendicitis. With a diet consisting of small amounts of rice, coarse vegetables and almost no meat or fats, such as was given to Dutch women and children in a Japanese internment camp, appendicitis almost disappeared. This would appear to indicate that there is a relation between diet, particularly the fat content and the incidence and mortality of appendicitis.—(*Arch. Chirurg. Neerland.*, 3, p. 164, Eng. Abst., *J.A.M.A.*, 19-1-'52).

FULL TERM BROAD LIGAMENT PREGNANCY

MISS PARVATI K. MALKANI, M.B., B.S., M.R.C.O.G.,

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PATIENT, M., aged 27 years was admitted to the hospital on 21st June 1951, with a history of vaginal bleeding for 2 days following an amenorrhœa of 5 months. Prior to this she had 4 menstrual periods which were scanty but at regular intervals of 28 days lasting for 4 to 5 days. Gradual enlargement of the abdomen had been noticed and foetal movements had been felt for the past 5 months but ceased 15 days back. She was getting regular, though scanty menstruation, and thought she was pregnant. She had some discomfort in the abdomen for one month and complained of pain in the back and abdomen simulating labour pains for the past 2 days. She was para 5+0, 5 full term normal deliveries, the last delivery being 21 months before.

General examination of the patient.—Patient looked pale, and seemed to have a moderate amount of pain in the abdomen. Temperature normal, pulse rapid 128/minute, respiration 20/minute, blood pressure 120/60 m.m. Hg. Tongue slightly coated. No abnormal signs in the chest. Breasts not active.

Blood examination :—Total R.B.C. 3 millions/c.m.m. Total W.B.C. 4,800/c.m.m. Differential count : polymorphs 60·0 per cent ; lymphocytes ; 38·0 per cent ; eosinophils 2·0 per cent ; haemoglobin 42 per cent ; C.S.R. 40 m.m./hr.

Abdominal examination :—A firm mass filling the abdomen from the symphysis pubis to the xiphisternum. No foetal parts could be palpated. A round mass about 3" in diameter was felt in the right iliac fossa. The mass seemed to get harder at shorter intervals and was thought to be the uterus undergoing contractions. Foetal movements could not be felt. Foetal heart sounds could not be heard. No tenderness anywhere.

Pelvic examination :—Cervix, soft, and pushed forwards behind the symphysis pubis. Body of the uterus could not be reached. A large firm mass was felt, filling the posterior fornix and this seemed to be continuous with the mass felt *per abdomen*. Foetal parts could not be felt. There was a slight discharge of dark blood on the fingers.

X-ray of abdomen was done on the same day. A foetus of about 40 weeks was lying across the abdomen transversely with the head in the left iliac fossa. There was over-lapping of bones suggestive of foetal death. Diagnosis of full term extra-uterine pregnancy was made.

Laparotomy was done on 23-6-'51. The abdomen was opened by a sub-umbilical median incision and a big mass came into view. As the extent of the mass was difficult to make out and there were

several thin adhesions, the incision was extended upwards by 2½". The adhesions were freed all round. There were 2 masses. The mass on the right side was the uterus enlarged to the size of about 10 weeks' pregnancy. Close to the left side of the uterus was a large firm mass filling the whole abdomen. The omentum and small bowel were adherent to this mass. A vertical incision about 4" long was made in the anterior wall of this mass and a macerated foetus of the size of about 40 weeks was extracted. The placenta was removed in 3 pieces. Some old blood came away from this cavity but there was no fresh bleeding on the posterior wall of this cavity; pelvic colon could be felt. Some gel-foam was left in the cavity and the incision in the wall of the cavity was closed with a continuous layer of No. 1 catgut.

The left tube and ovary could not be identified. The right tube and ovary were normal and the right tube was ligatured by Madelener's technique as the patient wished to be sterilised. The abdomen was closed. Blood transfusion ½ pint given during the operation. The patient left the operation theatre in good condition.

The post-operative convalescence was a stormy one. Maximum temperature rose up to 103°F during the first week, 102°F during the 2nd week, 100°F during the 3rd and 4th weeks, and gradually dropped to normal in the 5th week. A mass was felt on the left side of the abdomen which was increasing in size. The temperature did not drop even after the use of different antibiotics. On 8-7-'51 the mass was explored and drained. Blood-stained pus discharge came out. The temperature came down to normal but there was a rise of temperature again as the drainage ceased. The mass was drained a second time on 27-8-'51 and after that the patient made an uneventful recovery and was discharged from the hospital on 12-9-'51 in good condition.

Antibiotics for Underweight Infants

Answering a question whether aureomycin and chloromycetin (which have been successfully used to promote growth in poultry and animals) are likely to be useful in the treatment of retarded growth in children, who show no obvious endocrine disorder, the *British Medical Journal* for 3rd May 1952, states: "There have been no reports of the effect of chloromycetin on growth—but aureomycin has been found to make a marked difference in the weight-gain of infants suffering from fibrocystic disease of the pancreas. It has also been used for premature babies, and in a small series recently reported, the treated infants gained weight more rapidly than did the controls, perhaps because they were protected by the aureomycin from the infections which attacked a number of the controls."

These antibiotics are not without danger, especially in the youngest age groups, because of their interference with the normal vitamin synthesis in the gut and because of their effect on the mouth. Stomatitis and thrush have repeatedly occurred and the possibility of a generalised moniliasis must be borne in mind. Their use in the treatment of retarded growth in children is not advisable except perhaps in cases where chronic and repeated infection is clearly responsible for the retarded growth.—(*B.M.J.*, 3-5-'52, p. 985).

A CASE OF IRRITIS AFTER B.C.G. VACCINATION

S. C. ROY, M.B.,

(Gold Medalist), Ophthalmic Surgeon, L.M. Hospital, Asansol.

A. K. G., a Hindu male, 24 years old, came to me on 24-7-'51 with a history of redness, pain, watering and photophobia in the left eye for four days.

On examination, the following changes were found in the eye :—

1. *Conjunctiva* showed hyperæmia with circumcorneal injection.
2. *Cornea* showed a few discrete areas of infiltration at the upper part. These areas involved the layers of the cornea from the epithelium up to a major portion of the substantia propria. A few pannus ran from the limbus vertically down to these areas of infiltration.

The vessels of the pannus came from the limbus and were just under the epithelium of the cornea. There were 4 to 5 of these areas in all, each the size of a pin's head and each infiltrated area had a vessel running to it.

3. *Iris* was irregular and slightly contracted.

There were no precipitates on the back of the cornea and the anterior chamber was normal and the fluid not turbid. The sight in this eye was 6/36.

The other eye was normal.

There was adenitis of the left parotid region.

About a month and a half before the ocular symptoms started, the patient got a B.C.G. inoculation in his left arm on the deltoid region during a mass B.C.G. vaccination campaign in the coal field area of Asansol.

The inoculated spot on examination showed a persistent sinus oozing out some serous fluid.

Before he came to me, the patient received a course of penicillin injections and sulpha-drugs by mouth without any effect on the ocular symptoms.

Wassermann and Kahn's tests were negative.

He was put on salicylate mixture with hot compresses and atropine ointment to the eye.

During the next few days slight conjunctivitis occurred with a few minute ulcers of the cornea at the periphery. Antiseptic drops for the eye were used and also vitamin B₂ injections which were later omitted as these were excreted through the urine.

Two points arose for consideration in this connection *viz.*, (1) Could the iritis be the direct result of the B.C.G. inoculation? or (2) was it a manifestation of local allergy or hypersensitiveness due to the liberation of some unknown substances in the body on the impact of the B.C.G. inoculation? The latter was thought to be more probable and the patient was treated with calcium injections and an antihistaminic drug (antistine).

As the sinus on the arm healed, the eye also healed gradually; the degree of improvement in the two was so closely interrelated that the condition of the eye reflected the condition of the sinus in the arm and *vice versa*.

The patient made a gradual recovery and in 8 weeks' time the sinus, the keratitis and iritis all healed up simultaneously.

The vision in the left eye improved to 6/9.

Early Rising in Obstetrics and Gynaecology

Haultain and Irvine of the Bangour and Eastern General Hospitals, Edinburgh, record their observations on 1070 consecutive hospital and private obstetric cases, 28 caesarean sections, and 285 major abdominal and vaginal operations, in which early ambulation was practised. The patients were made to rise usually within twenty-four hours of, and certainly not later than thirty-six hours after delivery or operation. This was advantageous to them and no untoward complications occurred. The routine for puerperal cases was:—Patients who have had normal labours and spontaneous deliveries before 8 a.m., were allowed up for bed-making at 5 p.m.; on the 2nd day they were allowed up for meals and to go to the toilet; on the 3rd day they were allowed to handle their babies in the nursery; and from then onwards they were allowed up for a little longer each day, taking a bath on the 6th day and going home on the 10th day. Patients with perineal lacerations and episiotomies with sutures were treated no differently. They were swabbed twice daily by the nurse and sterile pads applied till the 7th day, when sutures are removed and a bath is taken. All patients have exercises for four days a week for half an hour daily. Only severe cardiac, and acute tuberculous cases, eclamptic and severe pre-eclamptic cases do not follow this routine. Women delivered by caesarean section are allowed up within 24 hours, but their movements are more restricted for 2 to 3 days. Usually they are allowed to go to the toilet on the 5th day. All the patients rest however, in bed for a considerable period every day.

Early rising did not interfere with the healing of the perineum and involution seemed to be accelerated. The persistence of red lochia may possibly be increased. In cases of pelvic floor-repair the healing of wounds was not influenced adversely by the early rising and catheterisation was far less often needed. The diminution in the use of bed-pans was appreciated by both patient and nurse. Early rising seemed to be of great benefit not only to the puerperal patients but also—even more—to the patients who had undergone major abdominal operations. In the U. S. A. the vogue for early ambulation was based chiefly on the presumption that thrombosis and embolism are greatly reduced by getting the patient up soon after operation. Haultain who went to U. S. A. in 1947 was very much impressed with the American practice and decided to give it a trial in his own practice at the hospital and in domiciliary treatment.—*The Lancet*, 6-10-'51, pp. 607-610.



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LEPROSY RELIEF AND CONTROL

(A BRIGHTER AND MORE CHEERFUL OUTLOOK)

AT a Conference of the Secretaries of the Kushta Nivarana Sangh (Leprosy Relief Association) held at the Rajaji Hall on Friday the 26th September, Hon. A. B. SHETTY, the Minister for Public Health in the Madras State referred to the treatment of leprosy and said that the new sulphone drugs are stated to be giving good results. The new treatment with these drugs has certainly created a new sense of hope in the minds of the patients and also of the doctors. "The happiest feature of leprosy work in the Madras State is the very close co-operation between voluntary agencies and the Government" said the Minister of Health. Speaking at a public meeting on the next day he stressed the importance of preventive measures and said that the Government had to provide greater facilities for the treatment of the disease by organising a network of treatment centres. The pilot scheme of Leprosy Control at Tirukoilur was intended to develop a pattern of co-ordinated control, the voluntary agencies working in close co-operation with the medical and public health departments of Government. A great deal of organisational and educational spade work has to be done to bring home to the minds of the people the importance of segregation, preventive measures and the removal of the unmerited social stigma that is attached to the unfortunate sufferers, through irrational fear.

Madras State has been far ahead of other states, also in the matter leprosy control. *The Leprosy Review* of London in a recent issue complimented Madras "as being more progressive in its outlook on leprosy than other parts of the world." Besides providing

facilities for leprosy treatment and research at two sanatoria and at various district and taluk hospitals and dispensaries, the State Government pays capitation grants to 19 sanatoria, 12 of which are run very efficiently by Christian missionaries and the rest by other private agencies. Five special clinics have been developed in the Tirukoilur Pilot Scheme of Leprosy Control, each village or group of villages looking after its own patients, their isolation etc. Mr. T. N. JAGADISAN, the enthusiastic Secretary of the Sangh is working as honorary organiser in that area. Like tuberculosis, leprosy has brought in its wake several social problems. Even if a specific and positively dependable cure for leprosy becomes available, we would not be able to solve all the problems. For every mutilated and crippled case, amongst the 12,00,000 patients suffering from Hansen's disease in our country, and every cured case not re-absorbed into useful employment in the community-set-up, should be considered as much a failure as any lack of success in our attempts to discover a specific cure for the disease. So the problem is two-fold :—(1) medical relief and successful treatment of the sufferers and (2) the rehabilitation of the mutilated victims of the scourge.

The sulphones mark a notable advance in the treatment of leprosy but at the same time they have several limitations, the greatest of which is the unduly long time taken for the complete elimination of the lepræ bacilli from the skin and nerves. It usually takes from 2 to 5 years for these acid-fast organisms to disappear from the skin lesions, and even then a few may lurk in the nerves. Again there are some cases that improve on sulphones, only up to a certain point and then remain stationary without further subsidence. Yet another limitation to sulphone therapy is 'the tendency to relapse when the drug is stopped after the arrest of the disease'. "This tendency is just becoming apparent" says Dr. DHARMENDRA, the renowned leprologist at the School of Tropical Medicine, Calcutta, "and may be noticed to a greater extent in future years." Inspite of all these limitations, the extensive use of sulphones is bound to have a far-reaching and beneficial effect in the arrest and control of the disease. The treatment with sulphones should include not only the hospitalized cases but also the very large out-patient population, who constitute the majority of sufferers and are liable to spread the infection. This is most essential in our country where, according to the Union Health Minister's estimate atleast 12,00,000 people suffer from this dire disease. The incidence is greatest in South and North Eastern India. Sulphone treatment, which a few years ago was somewhat expensive and used to cost Rs. 30 per patient per annum is now quite cheap and the average annual cost per patient is only Rs. 5.

Another great advance that has been made during the last few years is in the field of rehabilitative surgery for relieving the

deformity and disfigurements and for restoring the functions of the limbs injured and disabled by leprosy.

The patients are thus enabled to become as active as others. The Christian Medical College at Vellore is the pioneer in this orthopaedic aspect of leprosy and has made valuable contributions to reconstructive surgery which is rightly considered to be an essential and integral part of any rehabilitation programme in leprosy. Cosmetic procedures ranging from simple ear-repair to subcutaneous amputation of the breasts for gynaecomastia have been adopted in a few cases with significant success at the Lady Willingdon Leprosy Sanatorium at Tirumani near Chingleput. These procedures of reconstructive plastic surgery for the rehabilitation of deformed patients, are the result of several years' research work and experience of Dr. COCHRANE, Dr. PAUL of Tirumani and Dr. PAUL BRAND of Vellore; more recent rehabilitation procedures, like arthrodesis of small joints and tendon transplantations of the hand have been planned and are being practised under the auspices of the Hand Research Clinics both at Tirumani and at Vellore, under the direction of Dr. PAUL BRAND of the Christian Medical College at Vellore.

The outlook in the field of leprosy is thus becoming brighter and more hopeful than ever and we ourselves feel that the disease will gradually get under effective control and ultimately disappear from our midst, as it did in Europe and America in the eighteenth and early nineteenth centuries.

THE CURRENT STATUS OF ISONICOTINIC ACID HYDRAZIDES IN THE TREATMENT OF TUBERCULOSIS

ISONICOTINIC acid hydrazide also known as Iso-Niazid is a discovery for the treatment of tuberculosis, which comes in the wake of anti-tubercular drugs like Streptomycin and P.A.S. The name of the drug indicates the mother substance from which it is derived. It is closely related to nicotinic acid unlike which Iso-Niazid has remarkable anti-tubercular activity. Why nicotinic acid should be powerless against tuberculosis, while its derivative Iso-Niazid should be so potent has not been explained. Iso-Niazid is a white crystalline powder *available* in tablet form and when taken orally is *almost* completely absorbed from the intestinal tract. It is found in appreciable therapeutic concentrations in plasma, cerebro-spinal fluid and pleural exudates. As in the case of many other new antibiotics discovered in the last decade the anti-tubercular activity of Iso-Niazid was demonstrated *in vitro* before it was tried on human subjects.

The results of extensive trials on human subjects by several independent observers, have been unanimously in favour of the beneficial effect of this drug against human tuberculosis. In every case

the patient became afebrile within the first two weeks. This was found to occur independently of the nature of the tubercular lesion and the duration of the fever. From the point of view of the patient this aspect alone is very heartening. Most cases with highly toxic manifestations, were found to shed their toxicity in about 10 days. The previously dry and flaky appearance of the skin gave place to normal smooth oiliness and the general condition of the patient was found to have remarkably improved. The appetite also improved and nearly all the patients ate more food than before. The weight increased appreciably in all cases and this was certainly a welcome sign. The cough improved and the expectoration decreased considerably. This effect on the cough was noticeable by about the 2nd week. Patients whose sleep was greatly disturbed by bouts of coughing prior to the administration of Iso-Niazid, were able to rest more comfortably after its use. For purposes of prognosis, the most important item is the examination of sputum for the presence of the tubercle bacillus. In advanced exudative lesions, as well as in lesions with cavity, the sputum is invariably strongly positive for the bacillus. Observations for periods ranging from 4 to 15 weeks after the use of Iso-Niazid showed that an appreciable number of patients were expectorating sputum which was negative for tubercle bacillus. The number of such negative patients was greater with Iso-Niazid than with streptomycin or PAS. X-ray photographs taken before and after the use of this drug naturally showed improvement in the condition, depending on the extent of spread of the lesions before treatment was started. It would not be possible in a short note like this, to give fuller details of the improvement in this direction.

The dramatic claims once put forward regarding the value and specificity of streptomycin in tuberculosis have now become somewhat dulled by the remarkably high percentage of resistant strains that were found to develop in the course of the therapy. This resistance was countered by the simultaneous use of PAS along with streptomycin. Claims are now being made that Iso-Niazid gives rise to fewer resistant strains than the other two drugs. The question of drug-resistance can be decided only after prolonged use and so it is too early to come to any definite conclusions of value. Clinical trials of Iso-Niazid in human tuberculosis have shown fewer toxic symptoms than streptomycin. The vestibular disturbances observed in patients during streptomycin therapy due to its effect on the auditory nerve and the gastro-intestinal upsets caused by PAS are now sufficiently well-known. It is claimed for Iso-Niazid that neither of these major complications will arise. The few side-reactions that have been noticed so far, are largely related to the autonomic nervous system and consist of sympathetic stimulation. The symptoms noticed were constipation, bladder-sphincter disturbance and dryness of the mouth. Occasional vertigo and transitory fall in blood-pressure were also observed. The other

systems were found to be free from any involvement. The benefit from Iso-Niazid is not restricted to pulmonary tuberculosis alone. Its effect in tuberculous laryngitis, gastro-enteritis, and tuberculous otitis media is reported to be remarkable. It is claimed to be effective also against bone-tuberculosis. But this will have to be substantiated by extended trials over a longer period and any attempt at evaluating its efficacy at this stage will be premature.

The dosage generally recommended for Iso-Niazid is 3 to 5 mg. per kilogram of body-weight per day. This will work out to 150 to 300 mg. per day for an average adult. *Children with tuberculous meningitis have been treated with 5 to 7 mg. per kilogram of body-weight daily for 4 weeks or longer, without any apparent toxic effects.

In conclusion a note of warning has to be sounded in order to prevent any undue optimism about the efficacy of this new drug. Every new chemo-therapeutic agent is usually ushered in by the scientists with great optimism. Extensive clinical use of streptomycin and later of PAS, both of which were once thought to have definitely halted tuberculosis in its onward march has now proved that these drugs also have their limitations and cannot be considered specifics for the disease. It has become necessary in certain types of pulmonary tuberculosis, especially those with cavities to resort to the time-honoured orthodox methods of treatment, like artificial pneumothorax, (AP) pneumo-peritoneum (PP) and to surgical measures like thoracoplasty. The percentage of cases for which these measures have to be adopted, has now been greatly reduced, but one has to remember that chemotherapy alone cannot be relied upon to cure a protracted disease like tuberculosis.

Iso-Niazid is a new chemotherapeutic agent about whose efficacy we have still to know more, and about whose toxic symptoms we do not know much yet. Whether resistant-strains of tubercle bacilli will develop as the use of this new drug becomes more extensive, remains to be seen. These factors should receive sober and careful consideration, before we can accept it as a specific for tuberculosis. Till then, the use of Iso-Niazid will only be on intensive clinical trial.

HONORARY MEDICAL OFFICERS

THE system of Honorary Medical Officers was first introduced in the State hospitals in the City of Madras in 1923, during the Panagal Ministry and was extended to the moffussil in 1929; it was reorganized in 1938. It took some time after its first introduction, before the public, the paid hospital-staff and even the patients in the hospitals could reconcile themselves to and appreciate the services of these honorary officers, who without remuneration of any kind gave of their best to the sick, for ameliorating their sufferings.

* C.J. Modi—Isonicotinic Acid Hydrazide (Iso-Niazid) in Tuberculosis, I.J.M.S., July '52

Acting on the recommendations of the Medical Education Committee of 1947, the Madras State Government favoured the expansion of the Scheme of Honorary Medical Officers and increased their number by sanctioning additional posts for 11 Honorary Physicians, 17 Honorary Surgeons, and 137 Honorary Assistant Medical Officers. Inaugurating what was virtually a rejuvenated conference of the Honorary Medical Officers on the 27th September '52, Mr. A. B. SHETTY the State Health Minister paid a tribute to the valuable services rendered by the Honorary Medical Officers and said that Government wanted to expand the honorary system. At present they were having 10 Honorary (consulting) Surgeons and Physicians, 45 Honorary Surgeons and Physicians, and 326 Honorary Assistant Medical Officers. One third of the total number of honorary officers were serving in the State hospitals of the City. Mr. SHETTY further stated that except in the city and in a few places like Madhurai, Tiruchirappalli, Malabar, Coimbatore and Tanjore it was difficult to get a sufficient number of qualified doctors to run the special departments in hospitals.

The honorary system is advantageous both to the Government and to the officers serving in an honorary capacity in the hospitals. The existence of cordial relations between the honorary and the paid staff would alone make for efficiency and smooth working. Such cordial and friendly relations prevailed in the State hospitals of the City of Madras ; the same cannot however, be said of all the moffussil hospitals. The reason underlying such a state of affairs is in most cases, a lack of mutual understanding between the paid officer of Government at the head of affairs in the hospital and the Honorary Medical Officers. They should both realise that they are working for a humane and noble cause, *viz.*, alleviating human suffering. The Honorary Officer should feel that, though he is giving his services freely without any pecuniary benefit to himself, he should conform to the rules and discipline of the Institution to which he is attached and cooperate with the head of that Institution in maintaining order and discipline in the subordinate staff ; otherwise there is bound to be slackness and inefficiency which would be detrimental to the health and well-being of the patients. The Honorary Officers should even set an example to the paid staff by being punctual in their attendance and by keeping to regular hours. The head of the institution, the District Medical Officer or the Senior Medical Officer in charge of the hospital, should on his part, realise the value of a kind and human approach in all his dealings with the Honorary Officers. He should not feel jealous of the popularity, success or opulence of the Honorary Medical Officer who may command a large and lucrative practice and live in high style. Mutual adjustments in this matter will alone enable the establishment of cordial relations between them and ensure the smooth working of the honorary system. Dr. PAUL referred in his Presidential address to the fact that several posts, listed in the civil medical list reserved for honorary medical officers,

remained unfilled, and also stressed the need for the maintenance of discipline at all costs, if any tangible good is to be achieved. Lt. Col. C.R. KRISHNASWAMI, the Chairman of the Reception Committee welcomed the Minister of Health and the delegates and pointed out that the Honorary Medical Officers were on *a par* in all respects with the paid Civil Surgeons of Government and so even the slightest discrimination as regards their duties, privileges or rights would constitute an insult to their self-respect. He also pleaded that their claims for the grant of scholarships and fellowships should not be ignored by Government.

We are in full sympathy with both of these claims and consider that the Honorary Physicians and Surgeons are in no way inferior to the paid Civil Surgeons in point of status, ability, experience and integrity and are therefore, entitled to be treated by Government in every respect on the same footing as their paid Civil Surgeons. In the matter of scholarships also, we feel that travelling fellowships of short duration should be secured or granted for the Honorary Physicians and Surgeons under fifty years of age, and also to exceptionally well-qualified senior members amongst the Honorary Assistant Medical Officers, who may well be expected in course of time to take up the posts of Honorary Physicians and Surgeons in Government Hospitals. Such fellowships would certainly be of great educational value to the officers concerned and of practical benefit and advantage to the State Hospitals. Those officers who avail themselves of this concession will have an additional sense of moral obligation to render continued and efficient service to the institutions in which they are employed.

Mr. A. B. SHETTY regretted that the financial stringency did not permit Government to consider the question of giving an honorarium to the honorary medical staff. We are not at all enamoured of the suggestion made by Dr. PAUL for the grant of an honorarium; it is common knowledge, that once an emolument of any kind is attached or sanctioned to any office it ceases to be essentially honorary and will not attract the right type of men with integrity, experience and selfless devotion to duty; it may even descend to the level of many other jobs, in which unseemly competition and nepotism enter insidiously and wreck superb edifices.

Aureomycin and the Intestinal Flora

The diarrhoea observed in patients treated with aureomycin for a period of three or more days may not be a toxic manifestation of the drug, but rather an expression of the profound effect this drug has on the intestinal flora. In this respect, it is similar to terramycin or for that matter, any combination of chemotherapeutic agents that are markedly active against both gram-negative and gram-positive aerobic and anaerobic bacteria of which the intestinal flora are composed. Very often, patients treated with these broad-spectrum antibiotics for a period of three days or more show nothing but pure cultures of yeast in their stools. Not infrequently the stools become loose, lose their normal odour, and the patient complains of pruritus ani, which may in all probability be due to the abnormal shift of the bacterial flora to the acid-producing yeasts.—(Henry Welch in *Jour. Hist. Med. Allied Sci.* Summer, 1951).

MEDICINE AND THERAPEUTICS

Thiocyanates in hypertension.—The fact that thiocyanates, sympathectomy or other therapeutic measures are of value in some hypertensive patients imposes upon us the duty of trying to discover which patients may be expected to derive benefit from one or other method of treatment until such time as we discover a single method of treatment that is suitable for all. For this reason, Loyal Davis has recently (1952) provided a working hypothesis of such importance that his paper will probably rank as one of the major contributions of the year.

Davis supports the contention that hypertension arises as the result of an imbalance between the normally existing pressor mechanism supplied by adrenal function and the depressor mechanism supplied by hepatic function. He postulates that thiocyanates depress adrenal function, producing changes in the blood chemistry resembling those following adrenalectomy. The fact that thiocyanates have been observed to deplete certain granules in the adrenal cortex both in animals and humans supports this view. Furthermore, mild chronic insufficiency of the liver, induced by partial occlusion of the portal vein in dogs with experimental renal hypertension, also initiates a depletion of these adrenal granules, although the histological changes are a little different from those found after thiocyanate administration. By decreasing the function of the adrenal medulla, sympathectomy augments the action of the thiocyanates whose action is on the pressor mechanism of the cortex. This may account for the clinical observation that some hypertensives who are resistant to thiocyanate therapy respond to it after sympathectomy.

Six clinical groups of hypertension are defined by Davis, excluding the type in which primary unilateral renal diseases are causal:—

The *fluctuant* type occurs typically in the early twenties, is usually asymp-

tomatic and is often discovered at routine physical examination. Thiocyanates are effective but are usually not necessary.

The *plethoric* type occurs typically in the energetic, overweight business man. Headaches, vertigo and angina of effort are common symptoms. Provided that irreversible renal damage has not occurred, thiocyanates reduce the erythrocyte count and the blood viscosity, and bring about symptomatic improvement.

Menopausal hypertension is analogous to the plethoric type seen in the male. If stilboestrol and sedation are insufficient alone, thiocyanates are usually beneficial. In fact these patients often do well so long as they are brought safely through the menopausal period, the hypertension often burning itself out subsequently.

The *high diastolic* type is a very grave condition occurring most usually in males between the ages of 35 and 50. It is rapidly progressive and malignant hypertension may supervene suddenly and without warning. Cardiac failure, renal failure or a cerebral vascular accident usually supervenes within 5 years. Thiocyanates alone are either of temporary value—resistance soon being acquired—or of no value at all. Sympathectomy alone, irrespective of the extent of the operation, has no permanent effect on either the blood-pressure or the clinical course in this type. Since, however, it has been found that some patients who have been resistant to thiocyanates become sensitive after sympathectomy, it may well be that sympathectomy followed by thiocyanate therapy is the treatment of choice in this type at the present time.

Arteriosclerotic hypertension is characterised by a relatively high systolic and a relatively low diastolic pressure, the onset usually being between the ages of 50 and 60. The disease is compatible with a long and useful life,

but *small* doses of thiocyanates are often valuable for controlling cerebral symptoms such as headaches, vertigo and tinnitus. It is important to avoid too rapid a fall in blood-pressure in this type.

Malignant hypertension shows no response to thiocyanates. The rapidly progressive necrotising arteriolar disease which underlies this type is responsible for the extreme gravity of the condition and the early onset of renal failure with intense hypertensive symptoms, including convulsions and coma. Although sympathectomy may be of prophylactic value in preventing a progressive type of hypertension from entering the malignant phase, no really effective treatment for established malignant hypertension is yet known.

It may be said in criticism of the views expressed by Davis that virtually nothing has been added to our *a priori* knowledge of those basic disturbances in normal physiology of which an abnormally high blood-pressure is nothing more than *one* outward manifestation. Those of a more practical turn of mind will, nevertheless, recognise in this contribution a major step towards a more rational assessment of the extreme disagreeable symptoms of which the hypertensive patient complains and their subsequent relief.—*Medical World*, Aug. 15, 1952.

Treatment of pin-worm infection with Egrassin.—Goddard, R. F. and Brown, H. W., *Journal of Pediatrics*, 40, 467-473, April 1952.

When given for 2 days in a dosage of 1 gm. 3 times a day for adults, Egrassin (Thymol isoamylcarbamate) is approximately 40% effective in thread-worm infestation.

Antibiotics and fungus infections—Lipnik, M. J., Kligman, A. M., and Strauss, R. J., *Investigative Dermatology*, 18, 247-260, March 1952.

Fungus *candida albicans* was isolated from the mouth or rectum of 6 patients out of 42 who were treated with oral penicillin for at least four days. With aureomycin and chloromycetin, this

number was much higher 51 out of 63 developing moniliasis. Approximately 80% of the fungi isolated were *C. albicans*. Fungi could be isolated from only 7 out of 67 control cases. Thus, not only was there a much greater percentage of individuals given antibiotics harbouring the fungi, but in almost every case there were large numbers of organisms present, particularly in those given aureomycin and chloromycetin. In the test tube none of these antibiotics stimulate growth of *C. albicans*. Aureomycin capsules and dibasic calcium phosphate, one of the inert ingredients of the carrier present in aureomycin capsules for oral use, stimulated growth of *candida albicans* in the test tube.

Treatment of tape-worm with quinacrine hydrochloride.—Sodeman, W. A. and Jung, R. C., *J.A.M.A.*, 148, 285-286, Jan. 26, 1952.

The authors gave 6 to 12 tablets (0.6-1.2 gms.) Atabrine to 11 patients suffering from tape-worm infestation. Cleansing enema was given one hour before starting the treatment. 0.2 gm. was given with a little water every 5 minutes until the entire dose (consistent with age and weight of patient) had been given. If nausea developed, soda bicarb was given with subsequent doses. 2 to 4 hours after the last dose saline or castor oil purge followed. 10 patients passed the entire worm. The 11th patient did not respond to purgation, but a 2nd course of atabrine two months later was successful.

Isonicotinic acid derivatives in the treatment of tuberculosis.—Robitzek, E. H., Chicago Tubercle Society—T. B. institution meeting on 3-5-1952 through *Lancet*, 262-557, March 15, 1952.

Probably the first man to use Isonicotinic Acid Hydrazide in the treatment of human tuberculosis, Dr. Robitzek has treated 143 patients with oral Isonicotinic Acid Hydrazide. (2.10 mgm/kgm/day) or its isopropyl derivatives (8 mgm/kgm/day). 92 patients, all seriously ill, were selected for detailed study. All the cases had proved refractory to large doses of PAS and streptomycin and many had surgical treatment. Still

all the chest cases had positive sputa and bilateral cavities before the treatment was initiated. Improvement was rapid, dramatic in some cases and consisted of (1) normalization of temperature, (2) increase in weight and energy, and (3) decrease in the quantity of sputa and cough.

Persistent negative sputa and gastric washings were observed in 25 per cent of the patients and occasional negative sputa and gastric washings in 28 per cent of the patients with chest involvement. X-ray changes did not keep pace with this striking clinical improvement. However, there was complete closure of cavities in two patients and marked reduction in the size of the cavity in 33 patients. All the 10 cases with tuberculous laryngitis improved. The average weight gained was about 2 lbs. per week during a 12 week period.

Induction of artificial pneumothorax by lung puncture.—E. N. Moyes and J. K. Scott, *The Lancet*, p. 1278, June 28, 1952.

The authors describe the technique of induction of artificial pneumothorax by deliberately puncturing the lung with a fine-bore hypodermic needle size 14-18 and 2.5-3 cm., long, attached to a 2 ml. record syringe. The procedure leads to leakage of air from the alveoli into the intrapleural space. A chest X-ray is taken 24 hours later and an artificial pneumothorax is induced, the degree of this depending upon the collapse shown by radiography. When a collapse is seen 24 hours after deliberate lung puncture, artificial pneumothorax may be induced 24 hours later and if the intrapleural pressures are satisfactory 200 to 400 c.c. of air can usually be given.

The rationale of this procedure is based on the observations by Morgan in 1914, who declared that every initial induction of artificial pneumothorax damages the lung and it is only because of the leakage of alveolar air, that it is possible to obtain intrapleural manometric pressure readings. This view was supported by gas analysis results of Ornstein. 150 to 500 c.c. of air must be present in a free pleural space before a

pneumothorax is visible and the leakage from lung puncture continues from periods varying from 12 hours to several days. The first refill should not be given at a fixed time, but each case should be judged on its merits and particularly on the size of the pneumothorax at 24 hours. The authors consider this to be a simple, safe and effective procedure, less liable to complications than the orthodox method.

Effects of penicillin and broad-spectrum antibiotics on the emergence of a gram-negative bacillary flora in the upper respiratory tract of infants.—Mc. Curdy, Robert S. and Neter, Erwin, *Squibb Abstract Bulletin*, p. 669, June 11, 1952.

Penicillin was given alone and in combination with one of the broad-spectrum antibiotics, (aureomycin, chloromycetin and terramycin) to 107 infants to determine the emergence of a predominant gram-negative bacillary flora of the upper respiratory tract. Treated with penicillin alone, such a change of flora took place in 1/3 of the patients. When a broad-spectrum antibiotic was used together with penicillin, this occurred in 2/3 of the cases. If a broad-spectrum antibiotic was used exclusively the change in the flora occurred in 1/5 of the cases. The vast majority showed a change to *E. coli* and *A. aerogenes*. The change of flora took place in 18 out of 71 infants suffering from respiratory infections and in 14 out of 36 children suffering from other diseases. The change in flora may coincide with the reappearance of symptoms. From this it appears that the use in infants of penicillin in combination with broad-spectrum antibiotics is followed rather frequent by the emergence of predominant gram-negative bacteria in the upper respiratory tract.

The treatment of pre-eclamptic oedema with ion-exchange resins—Preliminary report.—Carvey, H. M., *J. Obst. Gynaec., Brit. Empire*, 59 : 67-76, February 1952.

Four pre-eclamptic patients with associated oedema not responding to bed-rest, sedation and a low sodium diet were

treated with carboxylic cation type of ion-exchange resin. A mixture of the potassium and the ammonium type was given in doses of about 15 to 17 gm. per day to the first three patients. The 4th received the ammonium type alone in doses 30 to 60 gm. per day. The treatment was stopped after a week due to nausea. The authors considered the reduction in oedema due to treatment to be more rapid than with other routine methods of treatment. The resin therapy helps to keep pre-eclampsia in check and enables the pregnancy to continue till the fetus is sufficiently developed to stand a reasonable chance of survival.

Clinical evaluation of certain bulk and irritant laxatives.—Cass, L. J. and Wolf, L. P., *Gastroenterology*, 20: 149-157, January 1952.

The authors have studied the purgative effect of psyllium seed coat preparations with or without carbohydrate or of methylcellulose in 101 patients with moderate to severe constipation. The patients had had previous treatments with cascara, milk of magnesia, mineral oil or Alophen. In the opinion of the authors the psyllium preparations were the most effective purgatives producing improvement in 75 to 83% of the patients with severe constipation. Methylcellulose given alone worsened most of the patients.

Stethoscope tubing (Letter to the Editor).—(*The Lancet*, page 1307, June 52, 1952).

The optimum diameter of the stethoscope tubing is independent of the nature of the material of which the tube is made. The smooth bore of the plastic tubes does not give it any advantage over rubber or metal tubing, because a layer of air always remains adherent to the surface of the tube and the eddy currents in this layer contribute to sound losses. The important thing about the tubing is that it should be thick enough to exclude extraneous noises. Metal is poor in this respect and consequently metal parts of the stethoscope should be as short as possible.

Death after chloromycetin—(Annotation *Br. Med. Jour.*, 23rd Aug. '52).

Reviewing the case reports of three cases, two from Doncaster and one from Manchester, of fatal aplastic anaemia after chloramphenicol in children, the *British Medical Journal* makes the following comments. Three children whose whooping cough was treated with chloramphenicol subsequently died with symptoms of aplastic anaemia. These are the first British records to set alongside the American experience recorded in a recent leading article on the danger of chloramphenicol (*Br. Med. Jour.*, 19th July 1952) and there is little doubt that other cases will be discovered, now that the alert has been given. Once again prolonged dosage may have had something to do with the aplasia since daily chloramphenicol was given for atleast 24 days in all the three cases. As we remarked before, *prolonged treatment must now be regarded as unwise*. The object of treatment should be "to eradicate the infection and if this has not been achieved within a week an explanation for failure should be sought and other measures adopted", and we suggested that where possible another antibiotic such as aureomycin should be used in place of the suspect drug. At the same time, it must be remembered that *the size of the risk is not yet known*. It is impossible to say how often or how rarely fatal complications may be expected to follow chloromycetin treatment until a large follow-up study has been carried out. The danger of agranulocytosis was certainly over-emphasized when the early sulphonamides and thiouracils came in, and perhaps the risk of aplastic anaemia is perhaps similarly being over-emphasized now. Until we know definitely however, extreme caution must be the order of the day. (The italics above are ours).

[Special note:—According to a report in the *New York Times*, (14-9-1952) all packages of chloramphenicol distributed in the United States of America, must now bear a special warning label to the effect "Warning: blood dyscrasias may be associated with intermittent or prolonged use. It is essential that adequate blood

studies be made". This ruling by the Food and Drug Administration, Washington, follows a nation-wide survey of blood disorder cases. Out of 410 cases reviewed by a Committee of the National Research Council, 177

were found to have been associated with the use of chloramphenicol. About half of these cases were fatal. Death was attributed to failure of haemopoiesis in the bone marrow.—*Br. Med. Jour.*, p. 409, 30-8-1952].

SURGERY

Nutritional substitution therapy : A new method which prevents prostatic surgery in benign physiological hypertrophy.—B. F. Sieve (*American Journal of Digestive Diseases*, 18:369, Dec. 1951) describes a method for the treatment of benign prostatic hypertrophy by which surgery can be avoided if the treatment is begun sufficiently early. Before beginning such therapy a complete and detailed medical history must be obtained in each case; careful physical examination must be made including examination of the prostate, with special attention to degree of enlargement, and the presence of irregularities or nodules; a digital rectal examination should always be done followed by proctoscopic or sigmoidoscopic examination if indicated. The necessary laboratory tests to be made include complete and differential blood counts; urine analysis (preferably of a twelve-hour night specimen); determination of fasting blood sugar, nonprotein nitrogen and cholesterol of the blood. Basal metabolism determinations are also necessary. Prostatic smears are examined after each massage if possible. The treatment consists in a careful regulation of the diet to insure adequate intake of carbohydrate, protein and fat, and also the accessory food factors, vitamins, hormones, amino acids and essential minerals. All foci of infection should be treated, including any such focus in the prostate gland. On beginning treatment parenteral administration of certain vitamins and hormones is usually necessary, as indicated by the results of the preliminary examination in each case; and prostatic massage is employed as necessary; occasional "booster courses" of parenteral treatment are given as the patient is kept under observation. In 100 cases treated by this method, operation for prostatic hypertrophy was rendered unnecessary

and the gland was restored to normal in 90 per cent, although early prostatic symptoms had developed in 20 per cent; 7 per cent of the patients did not continue therapy; and in 3 per cent the condition was too far advanced for preventive therapy to be successful. The youngest patient was fifteen years of age; in young patients the prostatic symptoms are usually due to infection. Four cases are reported in detail, representing age groups from twenty to seventy-one years of age and describing the method of treatment in each case; in 2 of these cases hypertrophy of the prostate was prevented; in one, the prostatic hypertrophy was satisfactorily reduced and no operation was indicated. The oldest patient had refused replacement therapy "until too late" and operation was necessary.—*Medical Times*, Aug. '52.

Solitary cyst of the kidney and its relationship to renal tumour.—Anthony Walsh (*British Journal of Urology*, 23:377, Dec. 1951) in a review of over 500 cases of solitary cyst of the kidney reported in the literature found a malignant tumour of the kidney to be present in 7 per cent; the incidence of tumour was much higher in those cases in which the contents of the cyst were hemorrhagic (30 per cent). In 17 cases of solitary cyst of the kidney collected by the author in the past three years, there was an associated hypernephroma in 2 cases. In 1 of these cases a parapelvic cyst was surrounded by a hypernephroma, and in the other case the cyst was in the upper pole of the hypernephroma. Cases have been reported in which a benign tumour is found in one part of the kidney and a solitary cyst in another part of the kidney; in such cases there is probably no etiologic relation between the two. But where a malignant tumour is closely associated,

there may be an etiologic relationship; in nearly all such cases the neoplasm "impinges" on the base of the cyst. For this reason, the author is of the opinion that if a diagnosis of solitary cyst of the kidney is made, the kidney should be explored. If the contents of the cyst are haemorrhagic, nephrectomy is "probably indicated," because of the high incidence of malignant tumour with haemorrhagic cysts. If the contents of the cyst is only a serous fluid, the cyst should be opened and its base carefully inspected and palpated. In some cases of associated cyst and tumour, the growth of the tumour has been unusually slow which may be due to interference with its nutrition by the "expanding" cyst.—*Medical Times*, Aug. '52.

The management of staghorn renal calculi.—C. L. Prince and associates (*American Surgeon*, 17:1057, Nov. 1951) report 61 cases of staghorn renal calculi; the most common symptom was pain over the kidney involved; 23 patients, however, did not have any pain; 5 complained only of "backache"; and in 5 the calculus itself did not cause symptoms, but symptoms due to renal or ureteral disease on the opposite side led to a diagnostic study, which resulted in the discovery of the calculus. In 39 cases the staghorn calculus was unilateral, and the opposite kidney was normal; in 5 of these cases operation was not advised because of the age of the patient, or some other condition contraindicating surgery; in 5 cases operation was advised but has not yet been done. In the 29 cases in which operation was done, nephrectomy was done in 21 cases and removal of the calculus by nephrolithotomy or pyelonephrolithotomy, or heminephrectomy in 8 cases; in 2 cases in which heminephrectomy was done the stone in one half of a horse-shoe kidney. There were no deaths in this series. In cases in which the opposite kidney is normal, nephrectomy is preferred in a large percentage of cases, because of the danger of recurrence of branched calculi or persistent infection after lithotomy, also because the immediate surgical mortality after nephrolithotomy or pyelonephrolithotomy is

usually higher than after nephrectomy. In 14 cases in the authors' series in which the calculus was unilateral, and the opposite kidney was diseased, surgery was not advised in one case, was advised in 13 cases and has so far been done in 11 cases. Sixteen operations have been done in these 11 cases, chiefly operations on the opposite kidney or ureter; operation was done on the kidney containing the staghorn calculus in only 4 cases; in 2 nephrolithotomy was done, and in 2 nephrectomy was done after operation had been done on the opposite side and when it was found the kidney containing the staghorn calculus had been completely destroyed. There was one death in this group, after ureterolithotomy on the opposite side. In 6 cases of bilateral staghorn calculi, one patient refused operation. Bilateral operation, nephrolithotomy or pyelonephrolithotomy has been done on both sides in 4 patients, and on one side in the fifth patient, who is now awaiting operation on the opposite kidney. There was no death in this group. As a rule operation was done first on the kidney showing the best function. Preoperative preparation, which is most important in these cases, included antibiotics, blood transfusions, intravenous fluids, vitamins, and restoration of acid-base balance. In 2 cases, a nephrectomy had been done many years previously, the staghorn calculus in the remaining kidney was successfully removed in each case. The results indicate that operation for removal of staghorn calculi should be done more frequently.—*Medical Times*, Aug. '52.

Neoplasms—expanding, infiltrating, metastasizing.—(Bela Halpert, *Surgery*, Vol 30, 2, pp. 401-402, 1951).

According to present knowledge, neoplasms are derived from cells of the individual, and the neoplastic cells are either of anlage or of body cell origin; the former arise from hitherto dormant cells left over in the process of evolution of the individual. Those of body cell origin arise from cells of the individual still capable of cell-division. There are however, neoplasms so undifferentiated that the cellular origin remains undetermined. In such cases, the cells multiply

and produce bizarre structures without showing any clues of their cellular origin.

Neoplasms may grow expansively like a toy-balloon pushing and compressing rather than invading the adjoining tissues. These differ from those growing *infiltratively*, extending with finger-like processes into surrounding tissues, invading and replacing them. The neoplasms whose cells become detached and are carried by the blood stream or lymph to distant parts of the body where they set up foci similar to the cancer at the site of origin are metastasizing neoplasms. These terms *expanding*, *infiltrating* and *metastasizing* neoplasms, express more exactly the behaviour of the neoplasm than do the terms benign and malignant and are therefore, to be preferred.

Whether a neoplasm is expanding, infiltrating or metastasizing is of immediate concern to those dealing with patients who have a neoplastic disease. The handling of an expanding neoplasm, is quite uncomplicated, as complete surgical removal will cure the condition. Infiltrating neoplasms, are also capable of being cured by surgical removal, particularly in their incipient stages when they are still *in situ*, that is, in or near the site where they originated. These may be destroyed by irradiation. If treated by either method, cure may be obtained only if all cancer-cells are completely removed or killed; when irradiation is used, an adequate killing dose must be applied over the whole area of involvement, within an orbit of uninvolved tissue. When treated surgically, the operator must keep outside the cancer field and remove the involved area within a zone of uninvolved tissue. Entering the cancer field and touring it or removing it by "controlled excision" with frozen section, is of questionable value to the patient. Transplantation of cancer cells inadvertently or experimentally has proved again and again that the rule of not entering the cancer field cannot be violated without very serious consequences to the patient.

Infiltrating neoplasms, after they have metastasized to regional lymph nodes can be cured only if the entire area of involvement is removed. In the case of a carcinoma, the site of involvement, the lymph nodes, and the path between the

two must be removed in contiguity. Often this may not be possible; following operation, irradiation of the area that may still contain cancer cells aims at the destruction of residual cancer cells.

At present infiltrating neoplasms which have metastasized very widely and to distant organs are not curable by any surgical procedure, now can they be cured by direct methods of irradiation. The hope for improved treatment lies perhaps in chemotherapy combined with isotopes.

Gelfoam in surgery.—Gelfoam is a sterile, pliable, non-antigenic, surgical sponge capable of absorbing and holding within its meshes many times its weight of whole blood. When implanted in tissues it is completely absorbed in from four to six weeks without inducing excessive scar tissue formation. It is prepared from specially treated and purified gelatin solution which is beaten to the desired porosity, dried, sectioned, packaged, sealed, and sterilized by dry heat.

Indications :—Gelfoam saturated with thrombin is an aid in providing hemostasis in many fields of surgery, since capillary oozing or bleeding from veins may be controlled instantly. In case of arterial bleeding, the pressure of the flow prevents the sponge from remaining securely anchored and bleeding is likely to continue.

In **neurosurgery** gelfoam saturated with a solution of thrombin has been found effective in (a) halting oozing from the dura under the edges of the boneflap, (b) repairing torn dural venous sinuses to which ligatures cannot or should not be applied, (c) controlling troublesome epidural bleeders in laminectomy or herniated disk operations, and (d) controlling osseous bleeding.

In **otolaryngology**: For eliminating post-operative bleeding in submucous resections, the sponge may be moistened with thrombin solution, or lightly coated with petrolatum. For prevention of bleeding following the removal of nasal polyps, gelfoam saturated with thrombin solution may be placed in the nose and the patient instructed to blow it out several hours later. Following mastoidectomy, the sponge moistened with

thrombin solution may be used to line the mastoid cavity and allowed to remain in place. As gelfoam will disintegrate, its removal is not required.

In bone surgery: Gelfoam wetted with thrombin solution may be employed for controlling bleeding from bone tissue. Unlike bone wax, gelfoam is readily absorbed and does not interfere with the healing process.

In malignancy: Bleeding is often difficult to stop by the usual type of packing. This is easily managed with gelfoam saturated with thrombin solution, which should not be disturbed but allowed to remain in place. It is fully absorbed.

In abdominal surgery: Gelfoam sponge saturated with thrombin solution is usually effective in stopping bleeding of denuded visceral surfaces, particularly of the gall bladder bed, spleen and kidney.

Storage and handling: Gelfoam may be stored indefinitely. Once the container is opened, the contents are liable to contamination. Gelfoam should be used on the day the container is opened and the unused contents discarded. Unused portions could be resterilized by dry-air heating for two hours at 290°F. (143°C). Sterilization by autoclaving cannot be employed.

Directions for using: Pieces of gelfoam, cut to the desired thickness, length and width, are placed in and moistened on all sides with a solution of thrombin of appropriate concentration. The material is then withdrawn, squeezed between gloved fingers to remove the air bubbles present in the meshes, replaced in the thrombin solution, and left there until needed.

(The sponge should immediately swell to its original size and shape. If it does not swell when dropped into the solution the second time, it should be removed and kneaded vigorously until all air is expelled and the sponge expands to its original shape when dropped in the solution. This is the most important point to remember in preparing the sponge for use).

The pieces of sponge are then left wet or blotted to dampness on gauze and applied to the bleeding point. It

should be held in place with a pledget of cotton or a small gauze-sponge which may be removed in from ten to fifteen seconds. Removal of the pledget of cotton or gauze is made easier by wetting it with a few drops of water to prevent pulling up the gelatin sponge which now encloses a firm clot. Suction may be applied advantageously over the pledget of cotton or gauze to draw blood into the gelfoam, where it mixes with the thrombin, promptly clots, and causes the sponge to adhere rapidly.

(While suction hastens clotting, it is not essential, since the gelfoam will draw up blood by capillary attraction and cause clotting satisfactorily. Usually the gelatin sponge with thrombin will stop bleeding at the first attempt; but if not, additional application should be made, using fresh pieces of sponge prepared as described above.)

When bleeding is controlled, the pieces of gelfoam should be left in place; otherwise bleeding may start again. Since the gelatin sponge causes but little more cellular infiltration than the blood clot, the wound may be closed over it.—*International Medical Abstract and Reviews*, May 1952.

Chloroform anaesthesia—the latest word.—(Annotation, *Lancet*, 29-9-'51).

For nearly 50 years chloroform has been viewed with the gravest suspicion by anesthetists, who have had their opinion continually reinforced and sustained by papers based on laboratory work giving clear evidence of the toxicity of this substance. The feeling is widespread that *to use chloroform when any other method is available borders on negligence*. This clinical view has been supported by frequent statements both from the *post-mortem* room and—more probably—in the Coroner's Court. In spite of all this, many general practitioners find in chloroform sufficient good to make it their standby. They will obtain some but not much encouragement from what Ralph Waters and his coworkers have stated in their recent book "Chloroform—A Study after 100 Years." The pharmacology and anesthetic properties of

chloroform have been investigated afresh under modern conditions and with modern methods of study. The effect of chloroform on each of the main body systems—the liver, the kidneys, the cardiovascular and the respiratory systems—are reviewed, and the authors discuss the place of chloroform in anaesthesia, using statistics gathered in the anaesthetic department at Madison. Their conclusions are not on the whole startling; they call attention to the great potency of chloroform, to the difficulty of controlling the vapour strength accurately with the apparatus available, and the unreliability of physical signs in estimating depth of anaesthesia clinically when these are checked against blood-levels of chloroform. The action of chloroform in depressing respiration, lowering blood pressure, and causing cardiac arrest are confirmed. In suggesting that the hypotensive effect of chloroform be used deliberately to control bleeding, Waters and his colleagues seem unaware that in England it has been used for that purpose for years in operations like mastectomy. But they make it perfectly clear that chloroform can only be administered safely when the administrator is "*keenly aware of what he is doing*". It does not alter the fact that Chloroform is a highly potent agent full of troubles and dangers for the unwary. Until there are accurate means of controlling the vapour strength, it will carry inherent hazards, even in the hands of a skilled anaesthetist.

Traumatic periostitis in young children—(*Jour. Paediat.*, 38, 184-190, 1951).

Barmeyer, Alderson and Cox describe the "*acute limping leg*" in young children—a common occurrence of early childhood. After an apparently trivial injury, an X-ray picture taken say 3 to 4 weeks later, often shows some ossification of the periosteum at the site of the injury; in an X-ray picture taken during the acute pain, nothing abnormal is usually found. But if X-rayed after the acute symptoms have passed off, the evidence of ossification becomes apparent. They consider this condition to be the result of mechanical separation of the periosteum by injury.

Pethidine in anaesthesia.—(Johnson, P. D., pp. 705-707, Butler, E. B., pp. 715-716, both in *B. M. J.*, 22-9-51, also annotations by editor, *B. M. J.*, 22-9-51.)

Dr. W. B. Neff of San Francisco first introduced pethidine into anaesthetic practice in 1947, and Musbin and Rendell Baker published in 1949 their results on the use of this drug in British surgical practice. The drug has since become as common in the anaesthetic room as in the obstetrical wards, being used as a substitute for morphine in pre-and post-operative medication, when vomiting is expected or has to be carefully avoided. It is administered intravenously during operation instead of the usual adjuvants to nitrous-oxide anaesthesia. Repeated small doses of thiopentone are often administered for this purpose. Both these are respiratory depressants but pethidine has a shorter action and does not produce the troublesome post-operative narcosis so common after larger doses of thiopentone. It does not produce a laryngeal spasm or restlessness etc. Dunbar Johnson adopted the use of pethidine in a series of more than 200 unselected cases, covering a variety of planned and emergency operations. Many of these were poor-risk cases of a high average age; the oldest was 98 and the youngest 12. After establishing anaesthesia with pethidine he maintained it with nitrous-oxide in a circle absorber, giving gallamine trichloride to achieve muscular relaxation if and when necessary. The average patient needed an initial dose of pethidine 50 mg. and a further 20 mg. every 20 minutes after that; a more uniform level of anaesthesia was obtained and less pethidine had to be injected when it was given by intravenous infusion at the rate of 1 mg. per minute. He found that a solution diluted to 5-10 mg. per cc. for intermittent intravenous injection or to 0.2 mg. per cc. for continuous administration by intravenous transfusion had no significant effect on the respiration. He describes his results as very good as compared to other forms of anaesthesia and he praises the rapid return to consciousness, the absence of respiratory depression, the bronchial relaxation and the

prolonged post-operative analgesia afforded by this technique.

Dr. E. Blanche Butler records, in the same issue of the *British Medical Journal*, a case of hypersensitivity to pethidine in a woman aged 28, in labour. The drug was given by intramuscular injection (100 mg.) at once. She suffered a fall in blood-pressure and oedema of the face; the maximum fall in B. P. of 20 mm. Hg. systolic and 15 mm. Hg. diastolic occurred 4 hours after the injection.

Cotton thread as suture material.—(Steele, J. D., and Glasson, L.G.G., *Surgery*, Vol. 30, 3, pp. 516-522).

Steele and Glasson, Surgeons of the Muirdale Sanatorium, Columbia Hospital, carried out a study of cotton threads, in order to ascertain whether certain inexpensive cotton threads could be used safely and satisfactorily as suture material.

Expensive and inexpensive cotton threads were used, (after testing all of them for their breaking points) in suturing separate halves of the wounds of 18 patients having first stage extrapleural thoracoplasties for pulmonary tuberculosis. When the second stage of the thoracoplasty was performed 20 days later, a sample of each thread embedded in muscle was removed. Tissue sections for microscopic examination were made and the reactions of the tissues of the same patient to different cotton sutures were compared. Inexpensive cotton suture materials were used in a series of 73 consecutive patients having 296 thoracoplasty stages. One brand of silk suture material was tested for comparison with cotton, as regards breaking points and diameters of various sizes.

A tremendous difference in price exists between the inexpensive threads and the one brand of expensive thread studied. One inexpensive (J and P Coates) regular sewing thread was sold at 5 cents for a 50 yard spool, while the expensive brand of different sizes was to be had at prices varying from 4 to 8 dollars per spool of 100 yards, that is nearly 40 to 80 times the cost of the inexpensive sewing thread.

Although the latter expensive thread was found to be slightly stronger in

relation to its diameter than the inexpensive threads tested, the authors feel that this advantage is so small that it is insignificant from a practical standpoint. There was no more tissue reaction to the inexpensive cotton threads than to the very highly expensive cotton thread. The authors conclude that (1) some brands of cotton thread of the inexpensive varieties, are as satisfactory for use as surgical suture material as expensive thread manufactured specifically for surgical use.

(2) Some of these inexpensive threads compare favourably with the more expensive threads as far as diameter, cotton content, breaking points and tissue reactions are concerned.

(3) Since the tensile strength of cotton thread is definitely greater when wet, it is recommended that sutures always be used wet in order to take advantage of this added strength.

(4) Cotton sutures may be sterilized by either autoclaving or boiling well if used wet.

(5). There is a tremendous difference in price between the expensive and inexpensive thread.

The co-existence of goitre and deaf-mutism.—(Friedler, O.P., *Surgery*, (St. Louis) Sepr. 1951 : pp. 496-500).

In the course of the last 20 years, it has become increasingly obvious that, just as diabetes is not a primary disease of the pancreas, goitre is not merely a primary affection of the thyroid gland. The role of the hypophyseal, hyper- or hypoactivity has come to the foreground, so that a number of symptoms formerly ascribed to thyroid malfunction, we now know, to be of pituitary origin. There remain however a number of symptoms associated with evidence of thyroid disease whose mechanism of development is unknown. One of these is deaf-mutism, which, though not commonly present, does show a definitely higher incidence in goitre patients than in the general population. In Switzerland, with a notoriously large number of goitre patients, the incidence of deaf-mutism ranged between 24 and 250 per 10,000. In India, Stott and Gupta reported in 1934 (*Ind. Jour.*

Med. Res.), on the incidence of endemic goitre and cretinism in one of the provinces; they found that the incidence of deaf-mutism was 23 per 10,000. Of these deaf-mutes, 90 per cent had also an enlarged thyroid gland. Mc. Garrison, stated that "87 per cent of all cretins are deaf mutes to a greater or lesser degree," and his work was in the Chitral and Gilgit valleys in India (*Lancet*, 2, 1908).

After reviewing the literature, Dr. Friedlier, Surgeon in the American University Hospital in Beirut, Lebanon records in detail the histories, of 5 cases of deaf-mutism in a series of 85 patients admitted to his hospital with a diagnosis of non-toxic goitre over a period of 5 years. This meant that 6 per cent of his goitre patients were also deaf-mutes. None of his patients showed evidence of cretinism or myxoedema. There are thus two different groups of patients (1) one in which goitre and cretinism are associated with deaf-mutism and (2) another in which the goitre and deaf-mutism are not associa-

ted with any mental changes or low basal metabolism rate.

The picture throughout in the 5 cases was characteristic of iodine deficiency; yet all the patients live in an area of Beirut—a sea coast town, where there is presumably an adequate supply of iodine in the food and water. The underlying mechanism of the condition is obviously therefore, an abnormally high iodine requirement.

The treatment for these cases was both medical and surgical. As in all other adolescent goitres, iodine therapy should be given a fair trial first and surgery resorted to if that fails. The relatively large incidence of carcinoma in the so-called nodular goitre of young patients, makes surgery imperative in every case which does not respond to iodine therapy.

As regards deaf-mutism much can be done if their mental level is normal. Special courses of lip-reading to enable patients to talk have been devised by Swiss specialists.

OBSTETRICS AND GYNÆCOLOGY

Cardiac disease in pregnancy.—(*Br. Med. Jour.*, 26 July 1952).

Dr. A. P. Barry of Dublin speaking at the joint session of the British and Irish Medical Associations held on 11th July 1952, at Dublin, said that 90 per cent of pregnant cardiac patients were rheumatic in origin. During pregnancy the characteristic murmur might not be apparent on many occasions even with the closest scrutiny. A careful examination of the heart should therefore, be made at each antenatal visit in all cases, but specially in those with a history of rheumatic carditis. He graded his patients according to the classification of the New York Heart Association. Of 266 cases of cardiac disease associated with pregnancy, admitted into the National Maternity Hospital, Dublin, since 1949, mitral stenosis with or without other lesions accounted for 247 cases. The maternal mortality was only 0.75%. He advised restriction of salt and fluid intake in all cases. Increased vigilance was suggested for

Grade I patients; Grade II patients should have 10 hours' rest at night and 2 hours' in the afternoon. Both these grades should be hospitalized 2 to 3 weeks before delivery. Every patient in Grades III and IV must be at absolute rest in hospital until some weeks after delivery. Should cardiac failure occur at any stage during pregnancy it should be treated medically; there was no need to destroy the normal foetus under these circumstances. Induction of labour during the last three weeks was foolish.

As for methods of delivery, Dr. Barry found that the worse the grading the easier was the delivery. In the management of the cardiac condition itself, there was no place for caesarean section. Morphine and pethidine should be used in the first stage, but inhalation analgesics should be avoided because of the dangers of hyperventilation. If there were failure in the first stage, the patient should be assisted by venesection, morphine digoxin, and

aminophylline; if response was poor labour should be terminated. Lower segment caesarean section under local analgesia might be used; but Dr. Barry had found that, since the head is usually low and the cervix soft and dilated, the latter could be incised and a forceps delivery performed. During the second stage, oxygen could be administered and forceps delivery carried out under local analgesia as soon as possible. The incidence of forceps delivery in his 266 cardiac cases was 12.7%, only about 5% higher than the general rate for the hospital. The cesarean section rate was 1.5%. The total foetal loss excluding abortions was 6.3%.

Post-partum haemorrhage was not discouraged, but breast-feeding was inadvisable. Valvotomy could be carried out at any stage of pregnancy, if the cardiologist considered it necessary. Drs. W. Somerville and P. Phillips took part in the discussion that followed.

Oestrogen therapy of functional dysmenorrhoea: analysis of clinical results.—W. J. Dignam, J. T. Wortham and E. C. Hamblen (*American Journal of Obstetrics and Gynecology*, 59: 1124, May 1950) report a study of 8 patients treated with oestrogens for the relief of functional dysmenorrhoea. Two of these patients had had dysmenorrhoea since the menarche; 5 had had dysmenorrhoea for two to six years, averaging 3.6 years; one had had dysmenorrhoea for two years, since the birth of her second child. The age of the patients at the time of their first visit to the clinic ranged from eighteen to thirty years, with an average of 21.8 years. Four of the patients were married, but only one had had children. In the treatment of these patients Premarin (conjugated oestrogens) was given from the fifth through the twenty-fourth day of the menstrual cycle; the plan of treatment was to determine the dosage which would relieve pain and suppress ovulation; later it was attempted to reduce the dosage until ovulation occurred but pain was relieved. The time of ovulation was determined by means of basal body temperature charts. The daily dosage of Premarin varied from the equivalent of 0.3125 to 3.75 mg. of sodium oestrone

sulphate. The 8 patients in this series were treated through a total of 29 menstrual cycles; 2 patients became pregnant during treatment, and the effect on pain was not reported in one cycle, so that the effect of treatment on pain was determined in 26 cycles. All patients given 3.75 mg. of conjugated oestrogens daily from the 5th to the 24th day of the menstrual cycle were entirely relieved of pain during the following menstrual period; the lower doses employed relieved pain approximately half the time. The effect of the oestrogens on ovulation was not so definite, doses of 0.625 mg. and 0.3125 mg. never suppressed ovulation; each of the doses above 0.625 mg. daily suppressed ovulation about half of the time; a dose that suppressed ovulation one month permitted it to take place another month. The 2 patients who became pregnant during treatment were taking the same dosage of oestrogen that had suppressed ovulation in previous months. With one possible exception (in a patient with anxiety hysteria) pain was completely relieved when ovulation was definitely suppressed.—*Medical Times*, October, 1950.

Maternal obstetrical paralysis.—Report of two cases.—Jeffery C. Spry Leverton Bristol, England. *J. Obst. & Gynaec., Brit. Emp.* 58:1019-24, Dec. 1951.

Two cases of maternal obstetrical paralysis are reported. The first patient was a primigravida of 21 years. On the day following a prolonged labour with forceps delivery, she complained of pain in her left calf muscles and was unable to dorsiflex or evert her left foot. A back splint brought relief from pain in three days, but there remained a palsy of the anterior tibial and perineal branches of the external popliteal nerve, although there was no objective loss of sensation in the limb. The use of the back splint was continued following discharge, except for a few hours daily. Intensive physiotherapy was administered, and after eight weeks she could walk without too great difficulty. After eight months the residual wasting of the muscles of the thigh and calf was only slight, eversion was normal, but

the power of dorsiflexion was not wholly restored. An X-ray of the pelvis revealed a shallow sacroiliac fossa especially on the left side. There was a lateral tilt of L_4 and L_5 with compensatory lumbo-sacral lordosis. Also the second patient complained of residual numbness in her right leg, two days after a forceps delivery under spinal anaesthesia. A paralysis of the anterior tibial nerve with foot drop had developed. With the same treatment, recovery proceeded slowly at first but was later satisfactory. In this case, the pelvic X-ray revealed considerable flattening and relative exposure of the sacroiliac joint region.

Obstetrical paralysis may develop antepartum, following normal delivery or breech presentation, and may be bilateral. Some cases showed involvement of the femoral nerve or the whole sciatic nerve. Etiologic theories include: (1) lumbosacral cord compression; (2) rotation of the sacrum; (3) intervertebral disk protrusion; (4) other conditions such as a maladjusted leg stirrup, or spinal anaesthesia with an especially high concentration in a particular portion of the cauda equina.

In the first case mentioned, the cause of the paralysis was probably a compression of the lumbosacral cord by the large head of the infant. In the second case, the cause might have been pressure on the lumbosacral cord, injury to the cord by the forceps, or backward rotation of the sacrum accentuated by a difficult forceps delivery through a contracted mid pelvic-strait. Insufficient attention is often given to the weight of infants in previous apparently normal deliveries. Obstetrical paralysis is very rare in comparison with the incidence of the suggested causative conditions (Quar. Rev. of Obst. and Gynaec., July 1952).

A new view of the use of dicumarol in the pregnant patient.—D. L. Adamson and associates (*Amer. Jour. of Obst. and Gynec.*, 59:498, March 1950) report the use of Dicumarol at the onset of labour or prior to labour in 15 pregnant women who gave a history of or showed evidence of venous disease. Previously Dicumarol had been given in the puerperium for the

prevention of thrombophlebitis and pulmonary emboli. In all cases the method of dicumarolization outlined by Allen and associates was strictly followed. On the basis of the results obtained in the 15 patients given Dicumarol before or at the onset of labour, the authors conclude that any patient who develops acute phlebothrombosis or thrombophlebitis should be hospitalized and given Dicumarol. Such patients, if not adequately dicumarolized at the onset of labour, and can safely be given 300 mg. Dicumarol immediately after the onset of labour, and should be kept dicumarolized for at least ten days after labour. Any pregnant patient who has not developed acute phlebothrombosis or thrombophlebitis during pregnancy, but who has venous disease or a history of venous disease should also be given dicumarol (300 mg.) at the onset of labour and also be kept dicumarolized for ten days after delivery. No increase in immediate or delayed postpartum bleeding has been observed in any patient given Dicumarol prior to or at the onset of labour. Such use of dicumarol, it has been found, markedly decreases the incidence of painful, swollen legs after delivery in women with venous complications of pregnancy, and "will probably decrease" the incidence of pulmonary emboli in pregnancy and the puerperium in women with venous disease.—*Medical Times*, Oct. 1950.

Adrenocorticotropic hormone (ACTH) in the aetiology of eclampsia.—S. S. Garret (*W. Jour. of Sur. Obs. and Gynaec.*, 58: 229, May 1950) presents a study of the "striking parallel" between the effects of the administration of ACTH and the changes seen in eclamptic toxæmia. In the first place it is noted that the renal damage characteristic of eclampsia is identical with that produced by the administration of ACTH or 11 desoxycorticosterone; the lesions in the heart, brain and liver are also closely similar. The effect of high sodium chloride intake on the kidneys is the same in eclamptic toxæmia as with the administration of ACTH or adrenocortical steroids. The blood chemistry in

toxaemia and in ACTH poisoning is also characterized by haemodilution and slight lowering of the albumin-globulin ratio; with a rise in the blood uric acid. In severe cases of toxæmia, the differential blood count is similar to that induced by ACTH. Women with toxæmia show an increased urinary excretion of corticosteroids such as follows the administration of ACTH. On the basis of these findings, the author concludes that "the primary

etiological factor" in a large percentage of cases of eclamptic toxæmia is the increased secretion of adrenocorticotrophic hormone (ACTH) due to hyper-activity of the pituitary. The author suggests that the use of testosterone and its conjugates should be the most effective treatment for eclampsia due to hyper-secretion of ACTH; other drugs of value would be NH_4Cl , chlorine and ascorbic acid.—*Medical Times*, Oct. 1950.

REVIEWS OF BOOKS

Clinical Therapeutics—By PRAN KUMAR GUHA, M.B., Major, I.M.S. (Retd.) Late Medical Specialist in the I.A.M.C., Assistant Visiting Physician, B.I. Therapeutic Ward, Sir Nilrathan Sircar Research Institute, R. G. Kar Medical College Hospitals, Calcutta. 462 pages. Published by Messrs. S. C. Sircar & Sons, 1-C, College Square, Calcutta. Price Rs. 12/-.

It is a good plan to combine pharmacology and therapeutics in any book dealing with the treatment of diseases. This has been followed, by Dr. Guha in this book. For convenience of study, the book has been divided into a number of chapters, each chapter dealing at length with a particular drug. The latest drugs like streptomycin, PAS, aureomycin and Chloramphenicol as also Terramycin have also been dealt with. The newer additions like folic acid, Androgens etc. have also been included. A separate chapter has been devoted for antihelmintic treatment and the drugs used therefor. An addendum at the end of the book deals with a variety of useful therapeutic measures as for example, Antabuse in chronic alcoholism, sulphones in leprosy, and cortisone and ACTH in several joint-diseases. Methods of immunisation against whooping cough and measles, the use of aureomycin in intestinal amoebiasis and ulcerative colitis, have also received attention.

The book has been neatly indexed and printed in clear, bold type and will be very useful to the general practitioner for ready reference.

Wounds of the Extremities in Military Surgery.—By OSCAR P. HAMPTON (Jr.) M.D., F.A.C.S., Instructor in Clinical Orthopaedic Surgery, Washington University, School of Medicine; Colonel U.S. Army Reserve; Civilian Consultant to the Surgeon-General Department of the Army; Chief, Orthopaedic Section, 21st General Hospital, 1942-43; Consultant in Orthopaedic Surgery, Mediterranean Theatre of Operations 1943-45, Chief, Orthopaedic Branch, Surgical Consultants' Division, Office of the Surgeon-General, U.S. Army 1946. (1951) with 131 illustrations, 434 pages. Published by the C. V. Mosby Company, St. Louis.

The author has presented in this book the various measures adopted in the management of surgical emergencies in modern warfare. For convenience of study the subject matter has been arranged in a number of chapters. The first chapter deals with an outline of the general measures followed in military surgery. This includes a general plan of the outlay of medical facilities extending from the actual battle front to the base hospital. The second chapter deals with First Aid and the methods of emergency splinting. The third and the fourth chapters deal with minor surgery at the front-line hospitals, and include methods for counteracting shock, resuscitation, blood transfusion, application of tourniquets, post-operative management etc. as well as reparative wound-surgery. The next 4 chapters deal with the surgical measures usually

adopted in medical camps, situated farther away from the battle-front and include special types of war injury, like vascular nerve injuries, compound fractures, wounds of the joints, amputations etc. The chapters on compound fractures and joint wounds are very well written and suitably illustrated with excellent photographs. Burns and trench-foot and the treatment for these conditions are detailed in two chapters. Wounds of the hand and anaerobic wound infections are dealt with in two

separate chapters. The latter is very well written and accords with the importance of the subject since contamination of wounds is of very common occurrence on the field of battle.

Printed in clear bold type on beautiful art paper and illustrated profusely by excellent photographs, and provided also with a clear index at the end, this book will be of great help to the orthopaedic surgeon.

U.V.R.

NEWS AND NOTES

Association of Military Surgeons of the United States

59th Annual Meeting at the Statler Hotel in Washington, D.C., on 17th, 18th and 19th, November 1952

The President of the above association has kindly extended an invitation to us to attend their 59th annual meeting. He has also desired us to announce the meeting in our columns so that a large number of representatives from our country may attend and participate in the momentous meeting. We do so with pleasure. We are also informed that the Chiefs of the Medical Services of our Army, Navy and Air Force have been specially invited through the Minister of Defence of our country, the invitation having been delivered by a courier to the Indian Ambassador in Washington.

The Association of Military Surgeons was founded in 1891 and includes many of the world's eminent military physicians amongst its members.

An outstanding scientific programme has been arranged for this year's meeting and the organisers look forward to a large number of representatives

from all the principal nations of the world.

It is expected that in addition to a large number of scientific papers, there will be a grand display of technical exhibits illustrating the latest medical advances in military medical science. Further a special convocation will be held on November 18th during which every delegate present from our country will be decorated with the medal and ribbon of the Society and will have conferred upon him the Honorary Membership of the Association. On November 20th and 21st an International Clinical Symposium has been arranged for the visitors from abroad in the various government hospitals and medical centres in the Washington area under the auspices of the Surgeons-General of the United States Army, Navy, Air Force and Public Health Services and the Medical Director of the Veterans Administration. We hope and trust that several members of the profession from our country will attend the meeting; and we wish the meeting every success. We hope to be able to publish a report of the proceedings in due course.

CORRIGENDA

The two news items published in our September issue of the ANTISEPTIC at page 743, headed respectively "Powerful New Drug Fights Malaria" and "Mepacrine helps relieve rheumatic pain" were both from the Bulletins of the British Information Services. The omission to mention the source in the last issue is regretted.—(ED. ANTISEPTIC).

The word "liviron" in the note on British Schering's gift to India Government—appearing at page 743 of our last issue (September '52) is a misprint for "iviron". The error is regretted.—(ED. ANTISEPTIC).

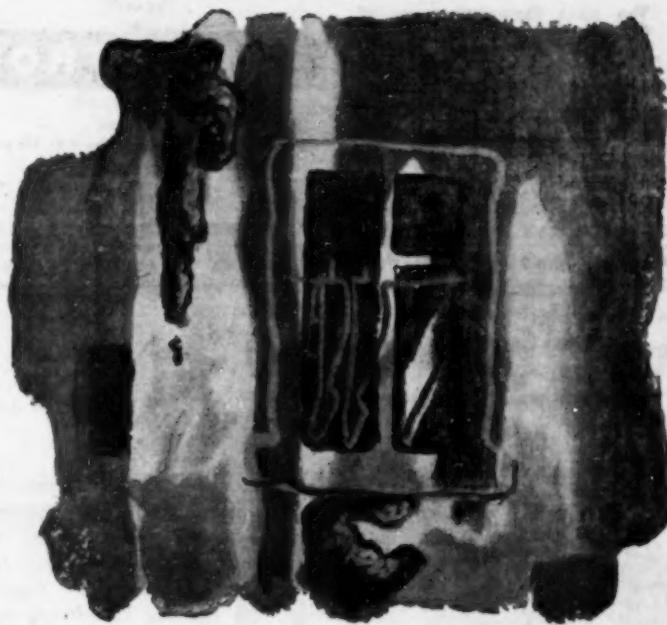


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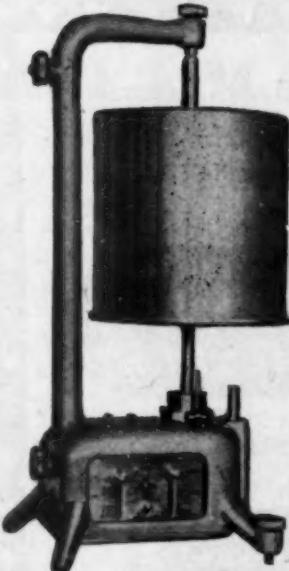
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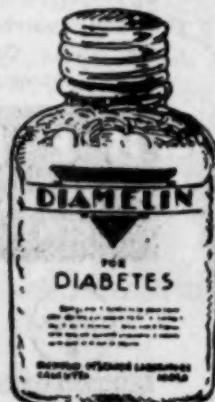
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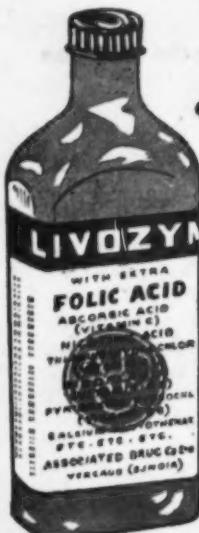
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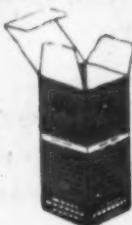
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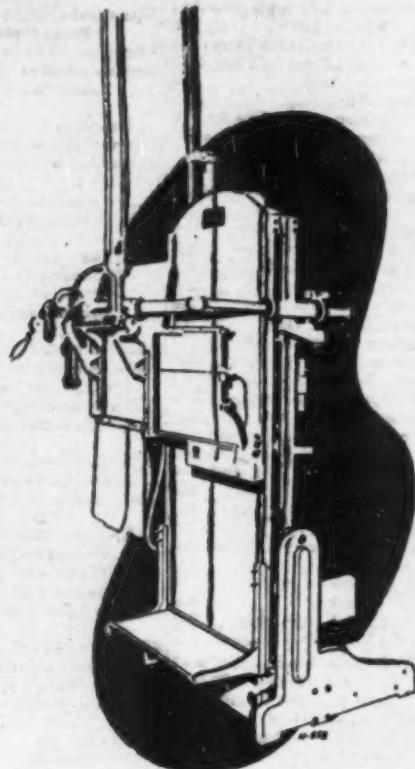
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SOME CASE REPORTS**Case 1**

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Age : 22, 2nd para. No secretion for about 3 wks., since delivery Breast not full but very thin discharge.

Treatment with LEPTADEX : 2 Tabs. of Leptaden T.D.S. on the 4th day secretion of milk produced but the infant suffered from diarrhoea, hence it was stopped (milk) but the treatment continued, relieving the breast by hands and after four days the child was put on breast. No diarrhoea.

Case 2

Care Dr. M.D.

Age : 26, 3rd. para. No secretion every time. Pt. diabetic. Soft breast and hardly any secretion.

Treatment with LEPTADEX : 2 T.D.S. on the 4th day of delivery. Responded.

Case 3

Care Dr. M.D.

Age : 32, 6th para. No secretion every time. No discharge nor tender and full breast.

Treatment with LEPTADEX : 2 T.D.S. responded after 4 days.

Case 4

Care Dr. M.D.

Age : 30, 5th para. Scanty secretion.

Treatment with LEPTADEX : 2 T.D.S. responded 2nd day.

Case 5

Care Dr. M.O., Maternity Hospital

Age : 35 yrs. Inability to suckle the baby. Dr. called in to see the patient on the 5th day after delivery. LEPTADEX (Alarsin) tablets 2 T.D.S. for one week, milk flow started on the 5th day of the treatment-continued 1 T.D.S. for another week and finally reduced to 1 tablet B.D. for one week more. The lactation period was uneventful.

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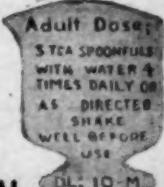
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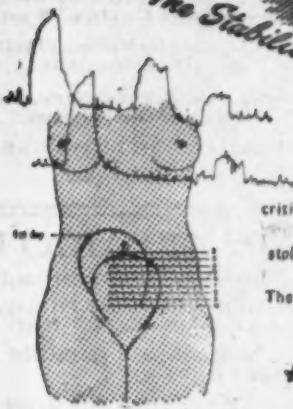
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.. 17-8 22-0 22-8 32-0 36-8	" cream 4 oz. Lilly 5-0 dos	" Italy 3-8 4-12 7-0 9-4 12-0
.. 11-8 14-8 15-0 100x5gr.x1cc.	Genital Violet Jilly 4 oz. Lilly 4-8	Boston 8-0 6-8 7-8 11-8 15-0
Equinine Whiffers 3-14; Java 4-6	Emetine amps. BDH 1/2 gr. x 12 7-8	R.D. Leck 8-0 11-0 13-8 16-0 23-0
Roche 4-12; Jap. 2-12	" 1 gr.x12 13-0; 1 gr. x 26 14-8	Japan .. 1-14 2-14 4-0 6-0 8-8
Q. Tab. 2grx100 2-2; 5gr 4-4 How	Endo 6 x 1/2 gr. 2-8	Italy M. case 1-2 1-8 2-0 2-6
.. 5 gr. 1400 How. 47-8	" P.D. 1/2 gr. 6cc 6-12 1 gr. 11-0	Metal case Ind. 50cc. 5-12
.. 5 gr x 1000 Germ. 32-8	B.W. 1/2 gr. 8-12; 1 gr. 3-0	Hypo Syringe 50 cc. S.N.
Bihydro 2grx100 3-0; 5gr 5-8 How	Ciba 250's 14-10; 20's 1-12	Jap. 5-0; Italy 10-8; Germ. 7-8
Pamaquinine 300 Tab. 0-12	CBaxol 250's 14-10; 20's 1-12	B.D. Luer Look 29-8; Jap. 14-8
Oral Tablets 1000 500 100	MB 760 27-12; MB 693 500's 40-8	Record Ger. 23-0; Italy 17-8
Asparine tab. 5-10; 1-4	First Aid Box 11-8; Amul Nit. cap2-0	Record Needles (Perfectum 5-4)
Mepacrine Eng. 10-4; ICI 12-8	Vitamin B tab. U.S.A. 500 1-12	Jap. Germ. Star. D.B. 14, 16
Quinacrine MB 13-12; 7-0	Liver Ext. 10cc. 2 USP P.D. 3-12	1-12 1-12 4-0 4-4 4-12 Dr.
.. USA. 5000 52-8; tin 1000 12-8	" Eng. 5 USP10cc. 4-6 20cc. 7-8	All Glass Needles Luer Mount
Ephedrin 1 gr. Gr. 1000 6-8; Ind. 5-12	Campomas 5x2cc. 5-8 25x2cc. 28-8	Jap. Ger. D.B. B.D.
Yeast Tab. Eng. 6-12; 7/ gr. 7-8	Cal. Glu. 10% x 10 cc. 100 13-8	2-8 3-4 5-8 9-8 dos.
Soda Mint .. 2-8; 100 0-12	Lucasol 25%x25cc.x100 21-0	Atebrin Amp 3 gr. 1 2 2-8 16-8
Paludrin 1000 1 gr. x 24-8	" Thilo Germ. 50 amp. 20-0	.. 0.1 grm. 8 2-6 [Teeth] forcep 4-8
.. 3 grm x 500 25-0; Strap.	Cysteprine I.V. I.M. Gr. 5-6 & Eng.	Camphor-in-Oil 3 gr. x1cc. x100
Aminophyllin Tab. 25 2-0 100 5-0	Atophanyl I.V. or I.M. 5-8 [4-10	W. Saline 100 x 5cc. 7-0 [Clip3-0
Ampas. 6x2cc 5-0; 0x10cc. 5-10	Atropine Sulf. 1 gr. 1-12	Omnopon Amps with Needle
Ext. Ergot. 4 oz 7-0 lb 18-8 Ind.	Calci Ostelin 15cc. 3-3 [100mg. 4-6	Nivaquin 10 1-12 [Tube 0-8
7 Son's Codiliver oil lb 7-0 1/2 4-4	NAB. 15's 0-10; 3 0-11; 45 0-13	F.L. Durex Tin. 3-0 dos. Pkt. 2-0
Sardine tab. 10 1-7; 250 25-4	Nicotinic Acid 500 3-0 [6-0 15	Ear, Metal Syringe 2oz. 5-8;
Petai Chiles 3-0; tab. 500 3-8	Nesalveras 0-15 30 45 60grs	Waterbury Co. 5-0 bot. [4oz. 6-12
Ind. Morph. Sulph. 1/2 gr x 20 2-8	[75grm. 1-12] 1-1 1-2 1-4 1-8	Vit. B12 Glaxo 20 mic. 6x1cc. 3-4
B.W. .. 1/2 gr x 20 5-0	Acetol Larson Adult 6-4 Child 4-12;	.. 50 mic. x 6 loc. 5-8; 5cc. 3-12
		Oil Chiaspidium st. 6-0 [10cc. 9-12
		Disp. Scale Nick 5-0; Brass 4-0



Rickets
Urticaria
Chilblains
Tuberculosis
Angioneurotic Oedema
Cæliac Disease
Osteomalacia
Hay Fever
Asthma

CALCIUM with VITAMIN D

For oral, intramuscular or subcutaneous use.

The oral product contains:
 0.85% colloidal calcium olate
 250 I.U. vitamin D per teaspoonful.

The injection product contains:
 0.85% colloidal calcium olate
 5,000 I.U. vitamin D per ml.

Recommended for the prophylaxis and treatment of rickets and osteomalacia; as an adjunct to treatment for pulmonary tuberculosis and celiac disease; and the control of dental caries. Has been used successfully in the treatment of neuro-circulatory disorders, such as chilblains, and angioneurotic oedema, for allergic conditions (urticaria, hay fever and asthma) and for controlling toxic symptoms resulting from heavy metal therapy.

PACKINGS. Oral 4 oz., 20 oz., 80 oz. bottles.
 Injection 1 ml., 2 ml. amps. 15 ml., 30 ml. R.C. vials.



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 IN THE
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A buffered, stable ophthalmic solution indicated in the treatment of bacterial and viral conjunctivitis, trachoma, keratitis and herpes zoster ophthalmicus. In vials of 15 c.c. capacity.



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